European Stroke Organisation Guidelines on the diagnosis and management of

Patent Foramen Ovale(PFO) after stroke

Valeria Caso , Guillaume Turc , Azmil H Abdul-Rahim, Pedro Castro, Salman Hussain,Avtar Lal, Heinrich Mattle, Eleni Korompoki , Lars Søndergaard, Danilo Toni, Silke Walter and Christian Pristipino

European Stroke Conference, Basel, 16.05.2024

Disclosures

Azmil H. Abdul-Rahim	1) Liverpool Centre for Cardiovascular Science at University of Liverpool, Liverpool John Moores University and Liverpool Heart & Chest Hospital, Liverpool, UK. 2) Department of Cardiovascular and Metabolic Medicine, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, UK. 3) Stroke Division, Department of Medicine for Older People, Whiston Hospital, Mersey and West Lancashire Teaching Hospitals NHS Trust, Prescot, UK.	**Intellectual disclosures:** Editorial board member for "European Stroke Journal" and "Stroke" **Financial disclosures:** None
Valeria Caso	Stroke Unit, Santa Maria della Misericordia Hospital-University of Perugia, Santa Maria della Misericordia Hospital -University of Perugia, Piazzale Giorgio Menghini, 3, 06129 Perugia Italy	No intellectual disclosure Financial disclosures: Advisory Board and speaker's honoraria: Bayer, BMS, Boehringer Ingelheim, Daichi-Sankyo, Pfizer All the honoria are paid to ARS UMBRIA Funded Research: European Union's Horizon 2020 research and innovation programme under grant agreement No 754517
Pedro Castro	Department of Neurology, Centro Hospitalar Universitário São João	None
Eleni Korompoki	Consultant of Internal Medicine, MD, PhD, FESO Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece	Speaker Honoraria/Travel grants: Bayer, Pfizer, Amgen, ELPEN, INNOVIS, Sanofi Funded Research: European Union's Horizon 2020 research and innovation programme under grant agreement No 754517
Heinrich Mattle	Neurologist, University Hospital for Neurology, Bern, Switzerland	Neurology principle investigator of the PC-Trial, member of the steering committee of the PRIMA Trial, consultancy fees from Medtronic, Stryker and Cerenovus
Christian Pristipino	S. Filippo Neri Hospital ASL Roma 1, Rome, Italy.	None
Lars Soendergaard	Chief Medical Officer and Divisional Vice President at Abbott Structural Heart, Medical Affairs, Santa Clara, USA	LS started his position in June 2023 and was not involved in the voting.
Danilo Toni	Neurology	No intellectual disclosure Finatial disclosures: Advisory Board and speaker's honoraria: Abbott, Alexion, Astra-Zeneca, Bayer, BMS, Boehringer Ingelheim, Daichi-Sankyo, Medtronic, Pfizer
Guillaume Turc	Department of Neurology, GHU Paris Psychiatrie et Neurosciences, Université de Paris, INSERM U1266, FHU NeuroVasc, Paris, France	lecturing fees from Guerbet France (unrelated to the present work)
Silke Walter	Department of Neurology, Saarland University and Department of Neurology, Martin-Luther-University, Halle, Germany	Intellectual disclosures: - Member at large ESO Executive Committee, - Board member of the Prehospital Stroke Treatment Organization (PRESTO) Financial disclosures: none
Salman Hussain	Methodologist, European Stroke Organisation, Basel, Switzerland	None
Avtar Lal	Methodologist, European Stroke Organisation, Basel, Switzerland	None

Module Working Group Members

Caso Valeria
Italy

Turc Guillaume, France

Abdul-Rahim, Azmil, UK

Castro Pedro, Portugal

Hussein Salman, Switzerland

Lal Avrtar, Switzerland

Søndergaard Lars, US A

Mattle Heinrich, Switzerland

Korompoki Eleni, Greece

Toni Danilio , Italy

Walter Silke, Germany

Pristipino Christian, Italy

PFO after Stroke

1.) PFO DIAGNOSIS

Overarching question: Which diagnostic test should be used to detect PFO-related right-to-left shunt in patients with cryptogenic stroke?

2.) TREATMENT OF PFO-ASSOCIATED STROKE

Overarching question: Which therapeutic strategy should be used in patients with PFO-associated stroke?

3.) POST-PROCEDURAL MANAGEMENT

What should be the long-term management after PFO closure in patients with cryptogenic stroke?

PFO DIAGNOSIS

- PICO 1.1 in patients with cryptogenic stroke, what is the diagnostic performance of c-TCD compared with c-TOE (conventional reference) to screen for a PFO related right-to-left shunt?

- PICO 1.2 In patients with cryptogenic stroke, what is the diagnostic performance of contrast-enhanced transthoracic echocardiogram (c-TTE) compared with contrast-enhanced transoesophageal echocardiogram (c-TOE, conventional reference) for identifying a PFO related right-to-left shunt?

- PICO 1.3: In patients with cryptogenic stroke, is the diagnostic performance of contrast-enhanced (c)-TCD superior to that of contrast-enhanced transthoracic echocardiogram (c-TTE) to screen for a PFO-related right-to-left shunt using contrast-enhanced transoesophageal echocardiogram (c-TOE) as conventional reference?

Evidence-based Recommendations Diagnosis

Overarching question: Which diagnostic test should be used to detect PFO-related right-to-left shunt in patients with cryptogenic stroke?

Evidence-based Recommendation for PICO 1.1, 1.2 and 1.3

In patients without an obvious cause of stroke, there is continued uncertainty over the most accurate diagnostic approach for detecting any RLS, because of the lack of a proper gold standard. Therefore, we are unable to offer an evidence-based recommendation.

Quality of evidence: **Very low** ⊕

Strength of recommendation: -

Expert Consensus Statement on Diagnosis

As there is no technique that can be considered as a gold standard, we advise locally agreed diagnostic algorithms using the available techniques (c-TCD, c-TTE and c-TOE) to diagnose an RLS, keeping into consideration that c-TCD is suggested when c-TTE and/or c-TOE are inconclusive. Vote: 8/9

In light of the available data, the MMG acknowledges that TCD demonstrates superior sensitivity relative to TTE in the RLS screening. Vote: 6/9

In patients without an obvious cause of stroke, but with positive diagnosis of RLS on initial assessment, we suggest TOE to gain additional information about the presence and anatomy of the PFO. Vote: 9/9

Supporting Information PICO 1.1
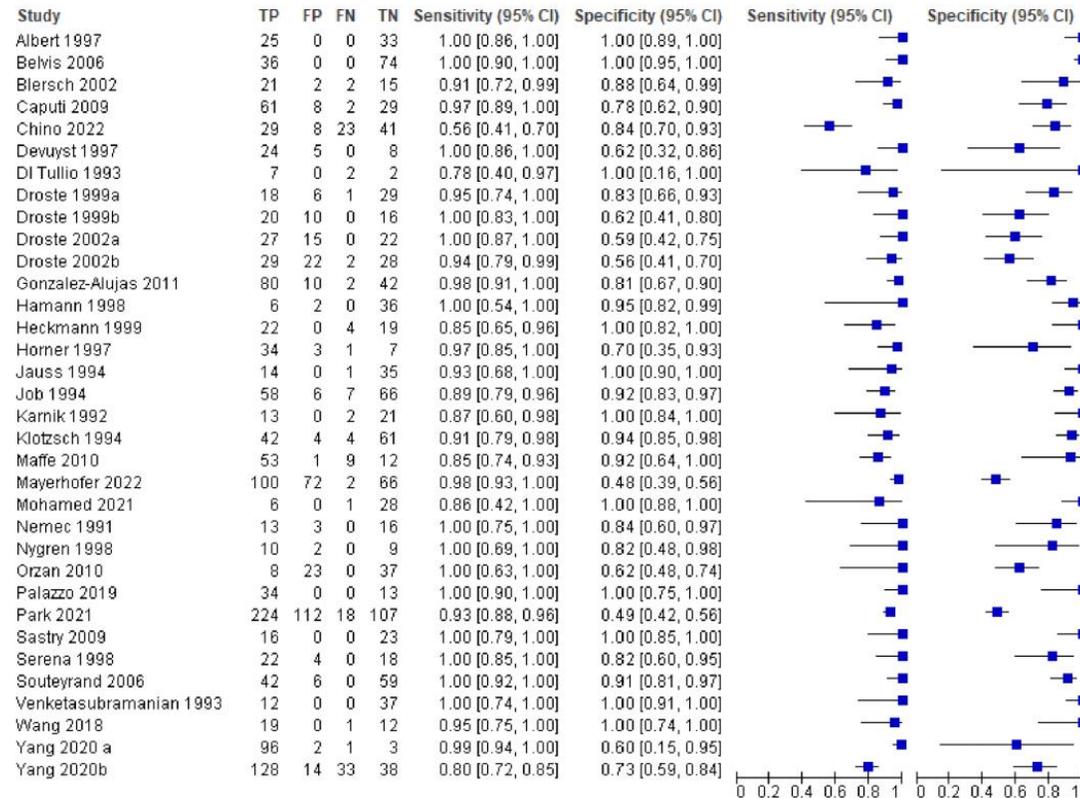
Figure 2. Risk of bias summary for PICO 1.1.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Albert 1997	25	0	0	33	1.00 [0.86, 1.00]	1.00 [0.89, 1.00]
Belvis 2006	36	0	0	74	1.00 [0.90, 1.00]	1.00 [0.95, 1.00]
Blersch 2002	21	2	2	15	0.91 [0.72, 0.99]	0.88 [0.64, 0.99]
Caputi 2009	61	8	2	29	0.97 [0.89, 1.00]	0.78 [0.62, 0.90]
Chino 2022	29	8	23	41	0.56 [0.41, 0.70]	0.84 [0.70, 0.93]
Devuyst 1997	24	5	0	8	1.00 [0.86, 1.00]	0.62 [0.32, 0.86]
DI Tullio 1993	7	0	2	2	0.78 [0.40, 0.97]	1.00 [0.16, 1.00]
Droste 1999a	18	6	1	29	0.95 [0.74, 1.00]	0.83 [0.66, 0.93]
Droste 1999b	20	10	0	16	1.00 [0.83, 1.00]	0.62 [0.41, 0.80]
Droste 2002a	27	15	0	22	1.00 [0.87, 1.00]	0.59 [0.42, 0.75]
Droste 2002b	29	22	2	28	0.94 [0.79, 0.99]	0.56 [0.41, 0.70]
Gonzalez-Alujas 2011	80	10	2	42	0.98 [0.91, 1.00]	0.81 [0.67, 0.90]
Hamann 1998	6	2	0	36	1.00 [0.54, 1.00]	0.95 [0.82, 0.99]
Heckmann 1999	22	0	4	19	0.85 [0.65, 0.96]	1.00 [0.82, 1.00]
Horner 1997	34	3	1	7	0.97 [0.85, 1.00]	0.70 [0.35, 0.93]
Jauss 1994	14	0	1	35	0.93 [0.68, 1.00]	1.00 [0.90, 1.00]
Job 1994	58	6	7	66	0.89 [0.79, 0.96]	0.92 [0.83, 0.97]
Karnik 1992	13	0	2	21	0.87 [0.60, 0.98]	1.00 [0.84, 1.00]
Klotzsch 1994	42	4	4	61	0.91 [0.79, 0.98]	0.94 [0.85, 0.98]
Maffe 2010	53	1	9	12	0.85 [0.74, 0.93]	0.92 [0.64, 1.00]
Mayerhofer 2022	100	72	2	66	0.98 [0.93, 1.00]	0.48 [0.39, 0.56]
Mohamed 2021	6	0	1	28	0.86 [0.42, 1.00]	1.00 [0.88, 1.00]
Nemec 1991	13	3	0	16	1.00 [0.75, 1.00]	0.84 [0.60, 0.97]
Nygren 1998	10	2	0	9	1.00 [0.69, 1.00]	0.82 [0.48, 0.98]
Orzan 2010	8	23	0	37	1.00 [0.63, 1.00]	0.62 [0.48, 0.74]
Palazzo 2019	34	0	0	13	1.00 [0.90, 1.00]	1.00 [0.75, 1.00]
Park 2021	224	112	18	107	0.93 [0.88, 0.96]	0.49 [0.42, 0.56]
Sastry 2009	16	0	0	23	1.00 [0.79, 1.00]	1.00 [0.85, 1.00]
Serena 1998	22	4	0	18	1.00 [0.85, 1.00]	0.82 [0.60, 0.95]
Souteyrand 2006	42	6	0	59	1.00 [0.92, 1.00]	0.91 [0.81, 0.97]
Venketasubramanian 1993	12	0	0	37	1.00 [0.74, 1.00]	1.00 [0.91, 1.00]
Wang 2018	19	0	1	12	0.95 [0.75, 1.00]	1.00 [0.74, 1.00]
Yang 2020 a	96	2	1	3	0.99 [0.94, 1.00]	0.60 [0.15, 0.95]
Yang 2020b	128	14	33	38	0.80 [0.72, 0.85]	0.73 [0.59, 0.84]

Figure 3. Random-effects meta-analysis comparing the assessment of a **right-to-left shunt** with **c-TCD to c-TOE** as a reference test in patients with ischaemic stroke, TIA, silent infarcts migraine and other neurological diseases.
Pooled sensitivity 0.96 (95% CI: 0.93–0.98).
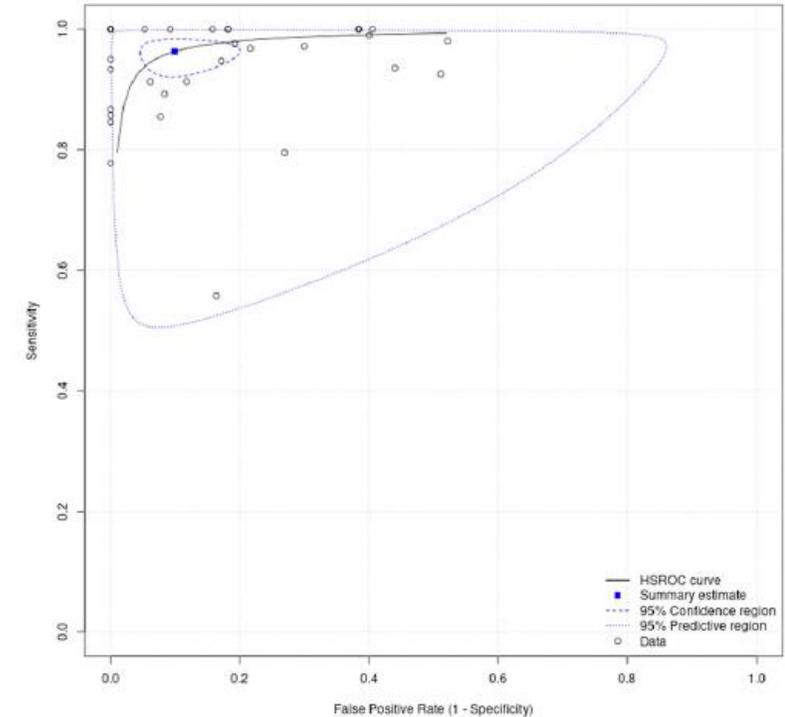Pooled specificity 0.90 (95% CI: 0.83–0.95).

Figure 4. Area under the summary receiver operating characteristic curve (sROC), reflecting the diagnostic accuracy for c-TCD and ROC curve displaying the average value of sensitivity of c-TCD over all possible values of specificity. The area under the ROC curve (AUC) is 0.96.

Supporting Information PICO 1.2, 1.3
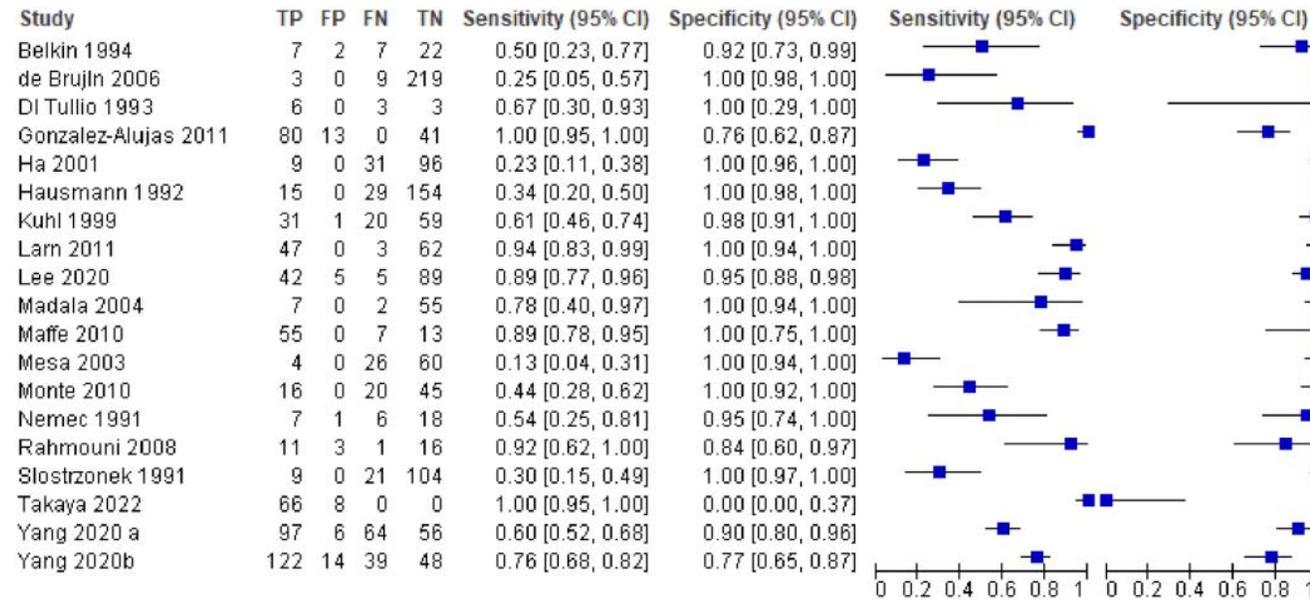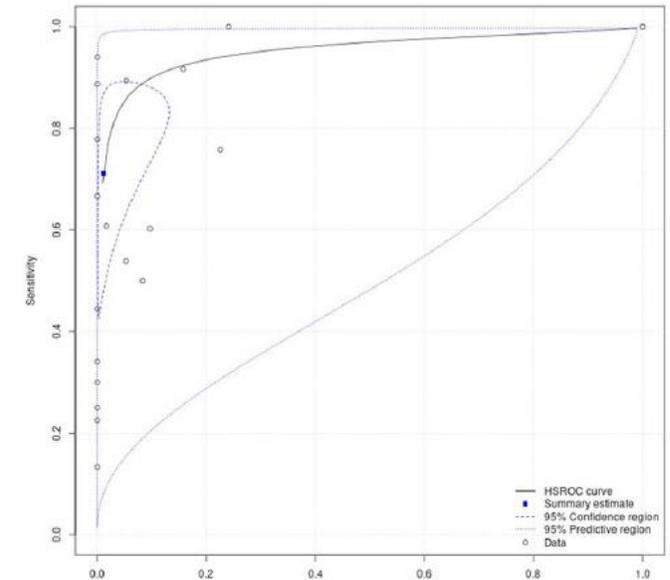
Figure 6. Risk of bias summary.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Belkin 1994	7	2	7	22	0.50 [0.23, 0.77]	0.92 [0.73, 0.99]
de Brujln 2006	3	0	9	219	0.25 [0.05, 0.57]	1.00 [0.98, 1.00]
DI Tullio 1993	6	0	3	3	0.67 [0.30, 0.93]	1.00 [0.29, 1.00]
Gonzalez-Alujas 2011	80	13	0	41	1.00 [0.95, 1.00]	0.76 [0.62, 0.87]
Ha 2001	9	0	31	96	0.23 [0.11, 0.38]	1.00 [0.96, 1.00]
Hausmann 1992	15	0	29	154	0.34 [0.20, 0.50]	1.00 [0.98, 1.00]
Kuhl 1999	31	1	20	59	0.61 [0.46, 0.74]	0.98 [0.91, 1.00]
Larn 2011	47	0	3	62	0.94 [0.83, 0.99]	1.00 [0.94, 1.00]
Lee 2020	42	5	5	89	0.89 [0.77, 0.96]	0.95 [0.88, 0.98]
Madala 2004	7	0	2	55	0.78 [0.40, 0.97]	1.00 [0.94, 1.00]
Maffe 2010	55	0	7	13	0.89 [0.78, 0.95]	1.00 [0.75, 1.00]
Mesa 2003	4	0	26	60	0.13 [0.04, 0.31]	1.00 [0.94, 1.00]
Monte 2010	16	0	20	45	0.44 [0.28, 0.62]	1.00 [0.92, 1.00]
Nemec 1991	7	1	6	18	0.54 [0.25, 0.81]	0.95 [0.74, 1.00]
Rahmouni 2008	11	3	1	16	0.92 [0.62, 1.00]	0.84 [0.60, 0.97]
Slostrzonek 1991	9	0	21	104	0.30 [0.15, 0.49]	1.00 [0.97, 1.00]
Takaya 2022	66	8	0	0	1.00 [0.95, 1.00]	0.00 [0.00, 0.37]
Yang 2020 a	97	6	64	56	0.60 [0.52, 0.68]	0.90 [0.80, 0.96]
Yang 2020b	122	14	39	48	0.76 [0.68, 0.82]	0.77 [0.65, 0.87]

Figure 7. Random-effects meta-analysis comparing the assessment of a **right-to-left shunt** with **c-TTE to c-TOE** as a reference test.
Pooled sensitivity: 0.71 (95% CI: 0.50–0.86).
Pooled specificity: 0.99 (95% CI: 0.93–1.00).

Figure 8. Area under the summary receiver operating characteristic curve (sROC), reflecting the diagnostic accuracy for c-TTE and ROC curve displaying the average value of sensitivity of c-TTE over all possible values of specificity. The area under the ROC curve (AUC) is 0.71, indicating an overall modest diagnostic accuracy of c-TTE.

PICO 1.3

The literature search did not identify any study comparing the diagnostic accuracy of c-TCD to c-TTE using c-TOE as the conventional reference for the detection of RLS.

PFO after Stroke

TREATMENT OF PFO-ASSOCIATED STROKE

Overarching question: Which therapeutic strategy should be used in patients with PFO-associated stroke?

2. In patients with cryptogenic stroke and PFO, does percutaneous closure of PFO plus antiplatelet therapy, as compared to antiplatelet therapy alone, reduce the risk of stroke recurrence?

Evidence-based Recommendations Treatment

PICO 2: In patients with cryptogenic stroke and PFO, does percutaneous closure of PFO plus antiplatelet therapy, as compared to antiplatelet therapy alone, reduce the risk of stroke recurrence?

Evidence-based Recommendation for PICO 2

In patients aged 18–60 years in whom no other evident cause of stroke is found but a PFO (i.e. PFO-associated stroke), we recommend PFO closure in selected patients, in addition to antiplatelet therapy (please see below for details).
Quality of evidence: High ⊕⊕⊕⊕
Strength of recommendation: Strong for intervention ↑↑

In patients aged 18–60 years with possible or probable PFO-related stroke according to the PASCAL classification, we recommend PFO closure in addition to antiplatelet therapy.
Quality of evidence: Moderate ⊕⊕⊕
Strength of recommendation: Strong for intervention ↑↑

Evidence-based Recommendations Treatment

PICO 2: In patients with cryptogenic stroke and PFO, does percutaneous closure of PFO plus antiplatelet therapy, as compared to antiplatelet therapy alone, reduce the risk of stroke recurrence?

Evidence-based Recommendation for PICO 2

In patients aged 18–60 years with unlikely PFO-related stroke according to the PASCAL classification, we suggest against PFO closure unless there is a high probability of clinical causality (please see the Expert consensus below).
Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak against intervention ↓?

In patients older than 60 and younger than 18 years, no evidence-based recommendation can be provided. Please see the expert consensus statements below.
Quality of evidence: Very Low ⊕
Strength of recommendation: -

Expert Consensus Statement on Treatment

Expert consensus statements on PFO closure in patients older than 60 years old and patients aged between 13 and 17

This panel encourages the inclusion of patients **older than 60 years old** with stroke and PFO in randomised trials whenever possible, or at least in a registry. If this is not possible, the majority of the module working group members suggest using the PASCAL Classification System and clinical judgement to guide therapy.

Vote: 8/9 experts agree

This panel suggests PFO closure in selected patients aged between 13 and 17 with PFO-related stroke according to PFO anatomy.

Vote: 9/9 experts agree

Given the lack of evidence for the timing of PFO closure, the panel suggests considering PFO closure within 6 months post-index stroke, based on randomised studies. However, as secondary prevention procedures are time-dependent, PFO closure should be performed as soon as possible based on each patient's clinical scenario, including stroke lesion size and risk profile.

Vote: 9/9 experts agree

Expert consensus statement on PFO closure in patients with unlikely PFO-related stroke according to the PASCAL classification

In patients aged 18–60 years with unlikely PFO-related stroke according to the PASCAL classification, this panel suggests PFO closure in various combinations of the following situations, which suggest a high probability of clinical causality:

non-cerebral embolism, deep venous thrombosis and/or pulmonary embolism close to index stroke, pulmonary arterial hypertension, history of sleep apnoea or other hypoxaemic conditions associated with PFO, Valsalva at stroke onset, recent history of prolonged immobility, recent airline travel, presence of venous thrombophilia, decompressive illness in divers, platypnea-orthodeoxia syndrome or a Eustachian valve or other anatomical features on echocardiography to enhance the risk of paradoxical embolism.

Vote: 7/9

ESO
EUROPEAN STROKE
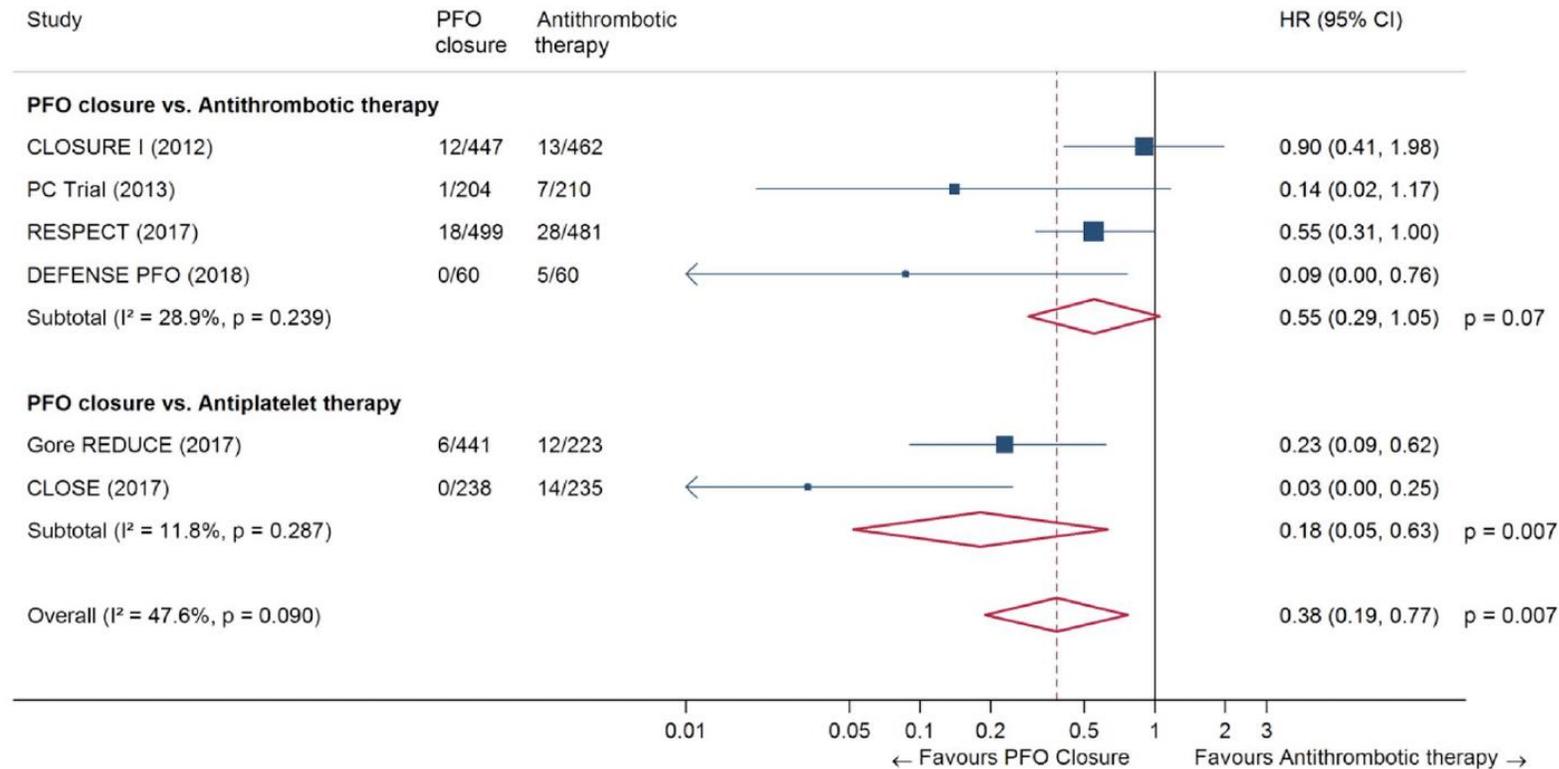ORGANISATION

Supporting Information PICO 2

Figure 9. Study-level meta-analysis of the risk of recurrent ischaemic stroke in patients with PFO-associated stroke and randomised to PFO closure versus medical therapy alone (updated from Turc et al.,[8] JAHA 2018 and Mas et al.[109]).

Supporting Information PICO 2

Table 6. RoPE score.[110]

Characteristic		Points
No history of	Hypertension	+1
	−Diabetes	+1
	− Stroke or transient ischaemic attack	+1
Non-smoker		+1
Cortical infarct on imaging		+1
Age (in years)	- 18–29	+5
	- 30–39	+4
	- 40–49	+3
	- 50–59	+2
	- 60–69	+1
	->70	+0
Total RoPE acore=sum of individual points (maximum = 10 points)		

Table 7. PASCAL classification system.[7]

High RoPE score (⩾7)	High-risk PFO feature (large shunt and/or ASA)[a]	Stroke related to PFO
Absent	Absent	Unlikely
Absent	Present	Possible
Present	Absent	Possible
Present	Present	Probable

[a]Large shunt size is defined as >20 bubbles in the left atrium on TOE; ASA defined as >10 mm of excursion from midline.

Table 8. Recurrent ischaemic stroke in the individual patient data meta-analysis[7,111].

Category		Hazard ratio (95% CI)	PFO closure, events at 2 years/ no of patients (%)	Medical therapy, events at 2 years/ no of patients (%)	Absolute risk reduction at 2 years	No. needed to treat at 2 years (95% CI)
PASCAL unlikely[a]	RoPE score <7, no large shunt, no ASA	1.14 (0.53–2.46)	11/293 (4.1)	8/254 (3.4)	−0.7 (−4.0 to 2.6)	−153 (−25 to 38)
PASCAL possible[a]	RoPE score ⩾7 or l arge shunt or ASA	0.038 (0.22–0.65)	13/897 (1.5)	31/914 (3.6)	2.1 (0.6–3.6)	47 (27–166)
PASCAL probable[a]	RoPE score ⩾7 and large shunt or ASA or both	0.10 (0.03–0.35)	2/700 (0.3)	16/683 (2.5)	2.1 (0.9–3.4)	47 (29–111)
PFO anatomy (disregarding RoPE score)[b]	large shunt and ASA[c]	0.15 (0.06–0.35)	0.4%	5.9%	5.5 (2.7–8.3)	18 (12–37)

PFO TREATMENT

- PICO 3: In patients with cryptogenic stroke and PFO, does percutaneous closure of the PFO plus antiplatelet therapy compared with oral anticoagulants (VKA or DOACs) reduce the risk of stroke recurrence?

Evidence-based Recommendations Treatment

PICO 3: In patients with cryptogenic stroke and PFO, does percutaneous closure of the PFO plus antiplatelet therapy compared with oral anticoagulants (VKA or DOACs) reduce the risk of stroke recurrence?

Evidence-based Recommendation for PICO 3

Evidence-based recommendation

In patients aged 18–60 years with possible or probable PFO-related stroke, there is insufficient evidence regarding the risks and benefits of long-term anticoagulation vs PFO closure. Nonetheless, we suggest PFO closure in addition to antiplatelet therapy rather than long-term oral anticoagulants alone, based on the (1) superiority of PFO closure over antithrombotic therapy demonstrated in the pivotal RCTs and (2) the cumulative risk of major bleedings associated with long-term anticoagulation.

Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak for intervention ⇑?
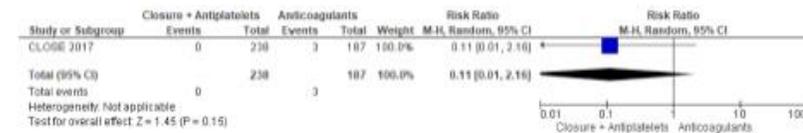
Figure 10. Risk of ischaemic stroke (only one study included).

Figure 11. Risk of death (only one study included).

Figure 12. Risk of TIA (only one study included).
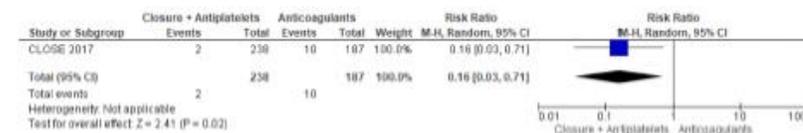
Evidence-based Recommendations Treatment and Consensus Statement

- PICO 4: In patients with cryptogenic stroke and PFO, does oral anticoagulation compared with antiplatelet therapy reduce the risk of recurrent stroke?

Evidence-based Recommendation and Consensus for PICO 4

There is continued uncertainty over the risks and benefits of the use of anticoagulation vs. antiplatelet therapy in patients in whom no other evident cause of stroke is found but a PFO (i.e., PFO-associated stroke).
Quality of evidence: Low ⊕⊕
Strength of recommendation: -

In light of the results of the meta-analyses including both randomised trials and observational studies, the majority of this panel suggest an individualised approach to the choice of antithrombotic therapy for patients with PFO-related stroke who refuse PFO closure. The choice of anticoagulation over antiplatelet therapy should balance the expected lower risk of PFO-related stroke recurrence with a possible increase in the long-term risk of major bleeding and take into account the patient's preference.
Vote: 9/9 experts agree

Supporting Information PICO 4

Figure 15. Risk of bias of randomised controlled trials.
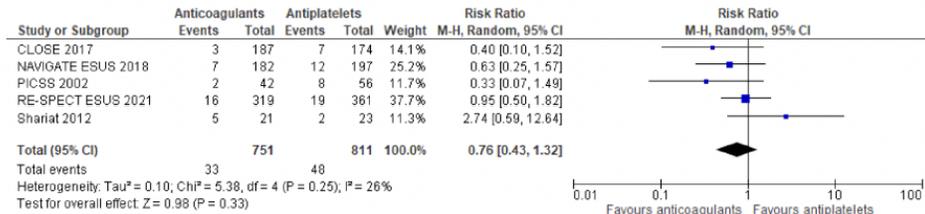

Figure 16. Risk of stroke recurrence restricted to RCTs (antiplatelets vs anticoagulants) stroke recurrence.
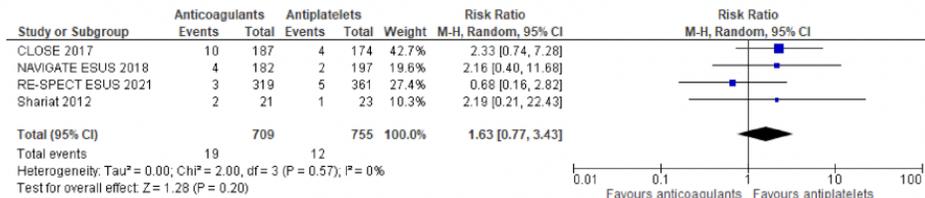

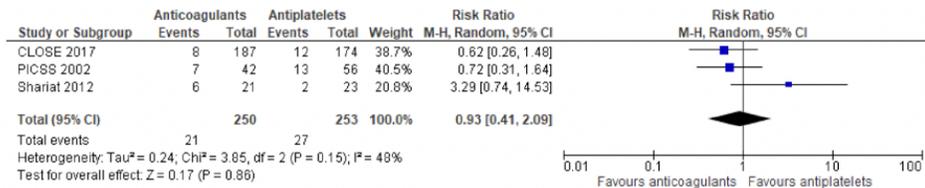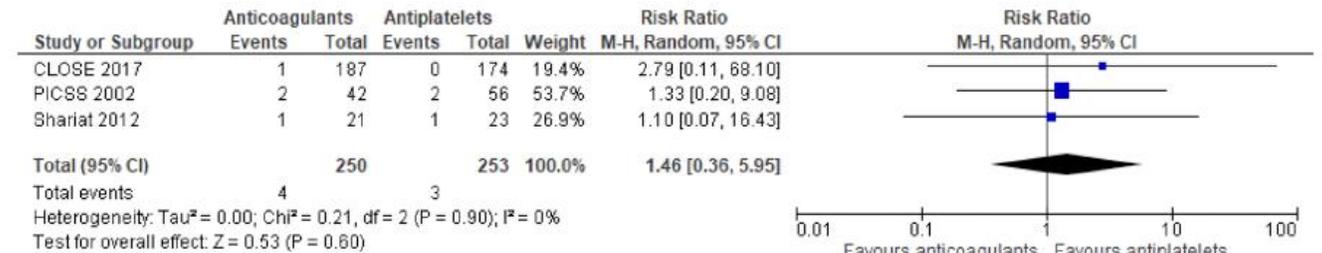Figure 17. Risk of major bleeding restricted to RCTs (antiplatelets vs anticoagulants).

Figure 18. Risk of composite outcome (stroke/TIA/death) restricted to RCTs (antiplatelets vs anticoagulants).

Figure 19. Risk of TIA restricted to RCTs (antiplatelets vs anticoagulants) TIA.

Evidence-based Recommendations and Consensus Statement on Longterm Management

- **PICO 5: After percutaneous closure in patients with PFO-related stroke, does dual antiplatelet therapy after the procedure compared with single antiplatelet therapy reduce the risk of recurrent stroke?**

Evidence-based Recommendation and Consensus for PICO 5

Evidence-based recommendation

There is continued uncertainty over the risks and benefits of the use of anticoagulation vs. antiplatelet therapy in patients in whom no other evident cause of stroke is found but a PFO (i.e., PFO-associated stroke). Please see the Expert Consensus Statement below.

Quality of evidence: Low ⊕⊕
Strength of recommendation: -

Expert consensus statement

In light of the results of the meta-analyses including both randomised trials and observational studies, we suggest an individualised approach to the choice of antithrombotic therapy for patients with PFO-related stroke who refuse PFO closure. The choice of anticoagulation over antiplatelet therapy should balance the expected lower risk of PFO-related stroke recurrence with a possible increase in the long-term risk of major bleeding and take into account the patient's preference.

Vote: 9/9 experts agree

Figure 21. Risk of bias assessment (ROBINS-I tool) of observational studies reporting data on dual antiplatelet therapy versus single antiplatelet therapy for reducing the risk of recurrent stroke after PFO closure.

Figure 22. Dual antiplatelet therapy versus single antiplatelet therapy and risk of recurrent stroke.

Figure 23. Dual antiplatelet therapy versus single antiplatelet therapy and risk of MI.

Evidence-based Recommendations Treatment and Consensus Statement

PICO 6:In patients with PFO-related stroke who have undergone percutaneous closure, does prolonged cardiac monitoring compared with no prolonged cardiac monitoring, reduce the risk of recurrent stroke?

Evidence-based Recommendation and Consensus for PICO 6

Evidence-based recommendations:

In patients aged 18–60 years in whom no other evident cause of stroke is found but a PFO, there is continued uncertainty over the risks and benefits of the use of long-term cardiac monitoring (i.e. ILR)

Please see the Expert Consensus Statement below.

Quality of evidence: Very Low ⊕
Strength of recommendation: –

Expert consensus statements

In line with the ESO guidelines on screening for AF after cryptogenic stroke,[142] this panel suggests that in patients <55 year old in whom no other evident cause of stroke is found but a PFO (i.e. PFO-associated stroke), a basic cardiac monitoring during 24 h by telemetry or Holter-ECG should be performed before closure.
Vote 8/9 experts agree

In line with the ESO guidelines on screening for atrial fibrillation after cryptogenic stroke,[142] we suggest using an ILR to detect paroxysmal AF in patients with cryptogenic stroke and PFO older than 60 years.
Vote 7/9 experts agree

We suggest that patients that have been implanted a loop recorder before PFO closure continue monitoring AF until the end-of-life of the recorder.
Vote 8/9 experts agree

We advise against systematic implantation of monitoring devices after PFO closure.
Vote 8/9 experts agree

We advise in favour of a systematic use of ILR in patients with recurrent stroke after PFO closure who have negative short-term ECG monitoring and no other obvious causes for recurrence, regardless of age.
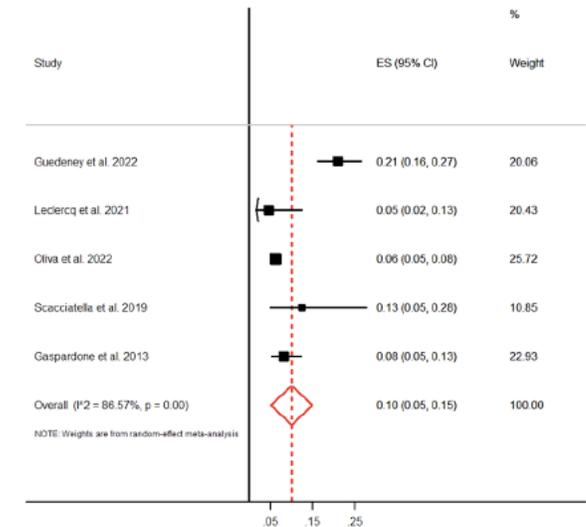Vote 8/9 experts agree

Study	ES (95% CI)	% Weight
Guedeney et al. 2022	0.21 (0.16, 0.27)	20.06
Leclercq et al. 2021	0.05 (0.02, 0.13)	20.43
Oliva et al. 2022	0.06 (0.05, 0.08)	25.72
Scacciatella et al. 2019	0.13 (0.05, 0.28)	10.85
Gaspardone et al. 2013	0.08 (0.05, 0.13)	22.93
Overall (I^2 = 86.57%, p = 0.00)	0.10 (0.05, 0.15)	100.00

NOTE: Weights are from random-effect meta-analysis

Figure 24. Meta-analysis of the incidence of AF after PFO closure in patients who underwent long-term cardiac monitoring.

Areas of future research

Diagnosis

Validation a gold standard for PFO Diagnosis

Validation of cardiac MR and cardiac CT

Treatment

- **PFO-related stroke during pregnancy**
- **PFO closure in <18 >60 year old patients**

Secondary Prevention

Management of Residual Right-Left-Shunt

-Duration of antiplatelet therapy after closure

Prognosis

-Systematic Prolonged cardiac Monitoring after PFO Closure

-Casual Role of late-onset AF

-Casual Role of Device detected AF

ESO
EUROPEAN STROKE
ORGANISATION

Conclusion

- Close PFO In patients aged 18–60 years in PFO-associated stroke in addition to DAPT for 6 months

- Use the PASCAL classification for Patient Selection for PFO Closure

- Randomize patients >60 in ongoing trials and registries

ESO
EUROPEAN STROKE
ORGANISATION