Universitäres Herzzentrum Hamburg

Controversies and key points for post-stroke white paper

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AF-SCREEN

Writing Group

N=38 researchers

Section	Lead	Topic
1	Maja-Lisa Løchen	Introduction, epidemiology, health problem
2	Hooman Kamel	Mechanisms and pathophysiology of atrial fibrillation & stroke
3	Giuseppe Boriani	Relevant atrial fibrillation
4	Tatjana Potpara	Therapeutic efficacy in stroke risk reduction
5	George Ntaios	Strategy to treat all ESUS with OAC vs only those with AF
6	Derk W. Krieger	When to initiate oral anticoagulation for AF after stroke/TIA?
7	Karl Georg Häusler	Whom to screen
8	Rolf Wachter	How to screen (method/device, setting)
9	Joseph Harbison	Cost-effectiveness of post stroke AF screening

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Writing Group

18 Key Points

N=38 researchers

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3 options for logging in to our interactive polls:

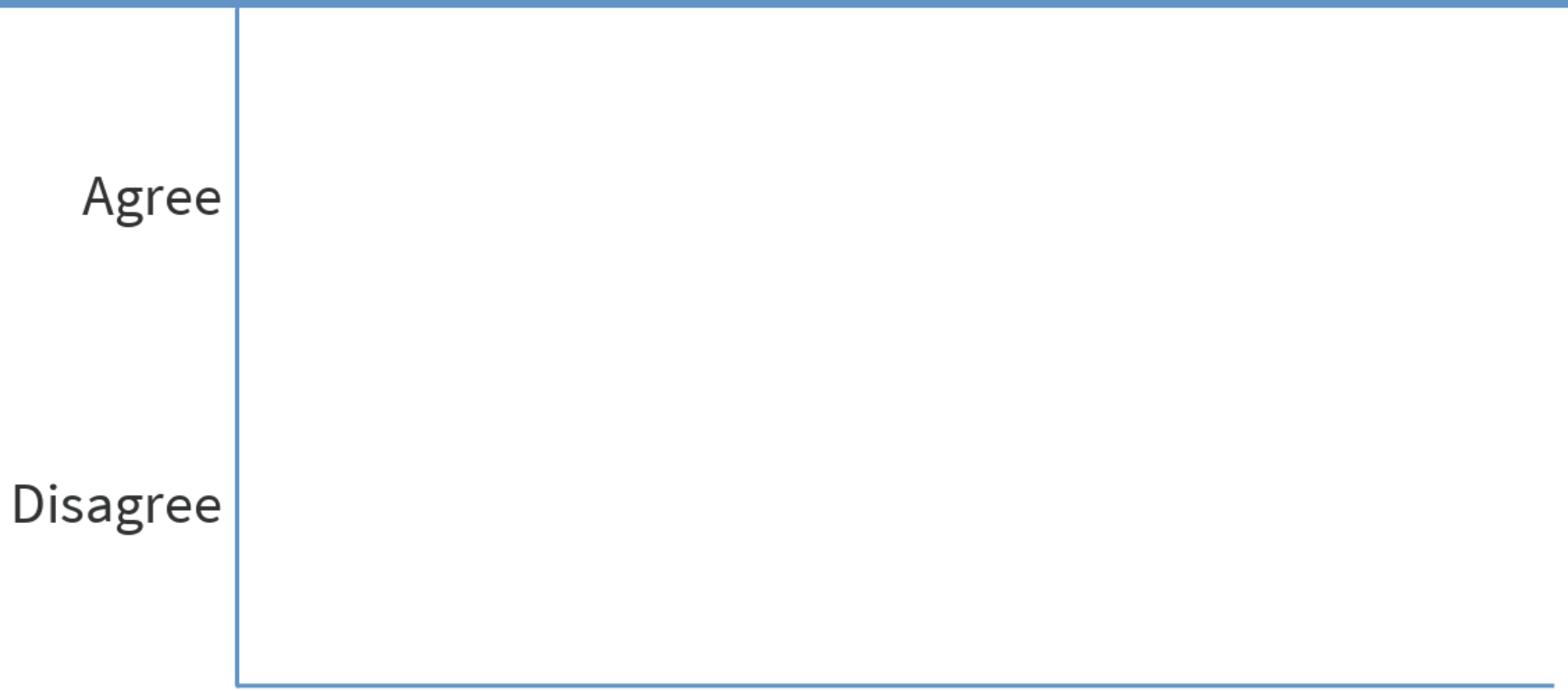
What Country are you from?

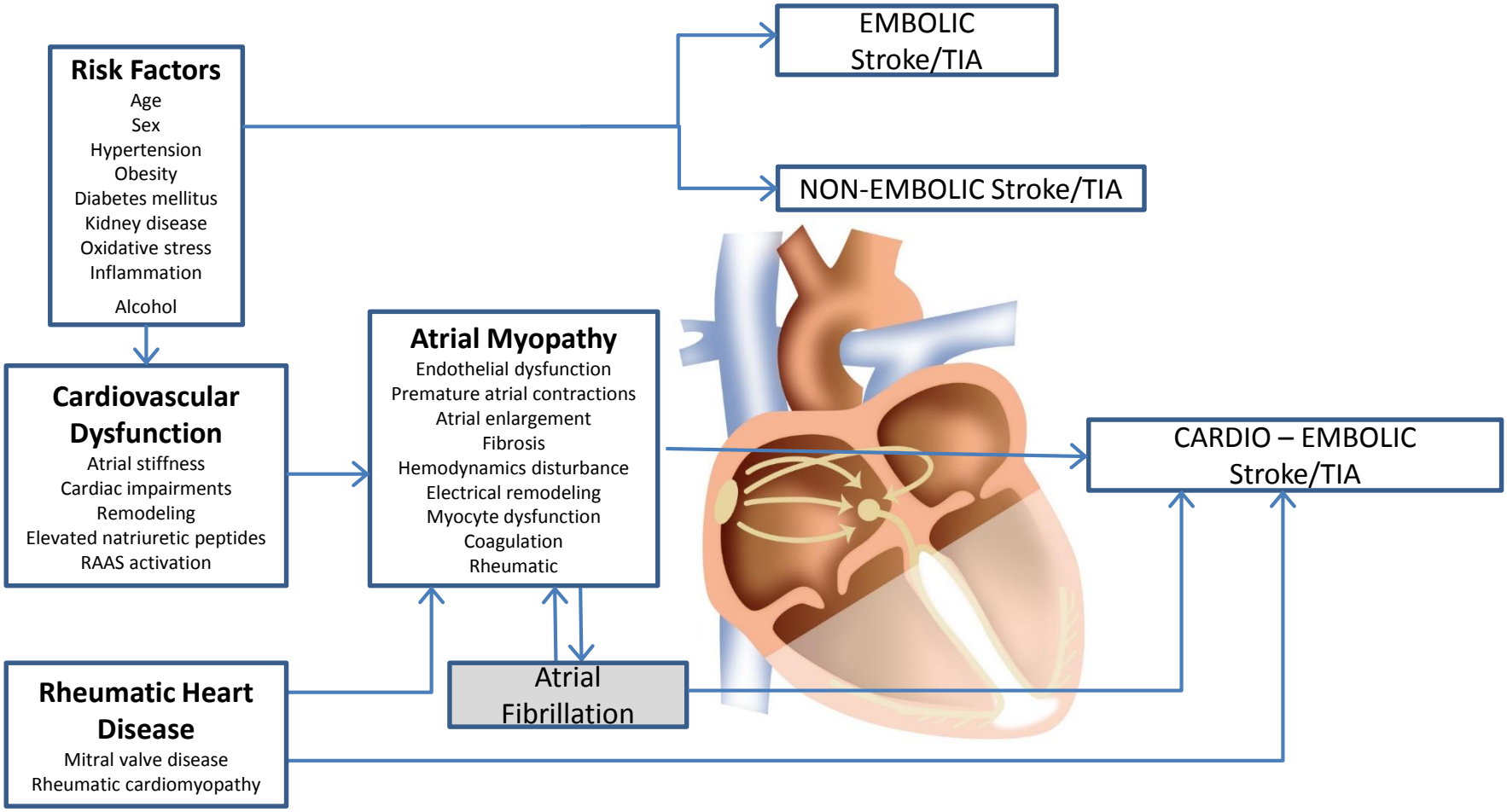
Key Point 1 Atrial Myopathy

Atrial fibrillation remains a strong marker for atrial myopathy and risk of thromboembolism.

Studies on post stroke AF screening and secondary stroke prevention should consider incorporating objective measures of atrial myopathy in addition to other risk factors.

Key point #1. Atrial Myopathy. Atrial fibrillation remains a strong marker for atrial myopathy and risk of thromboembolism. Studies on post stroke AF screening and secondary stroke prevention should consider incorporating measures of atrial myopathy in addition to other risk factors.

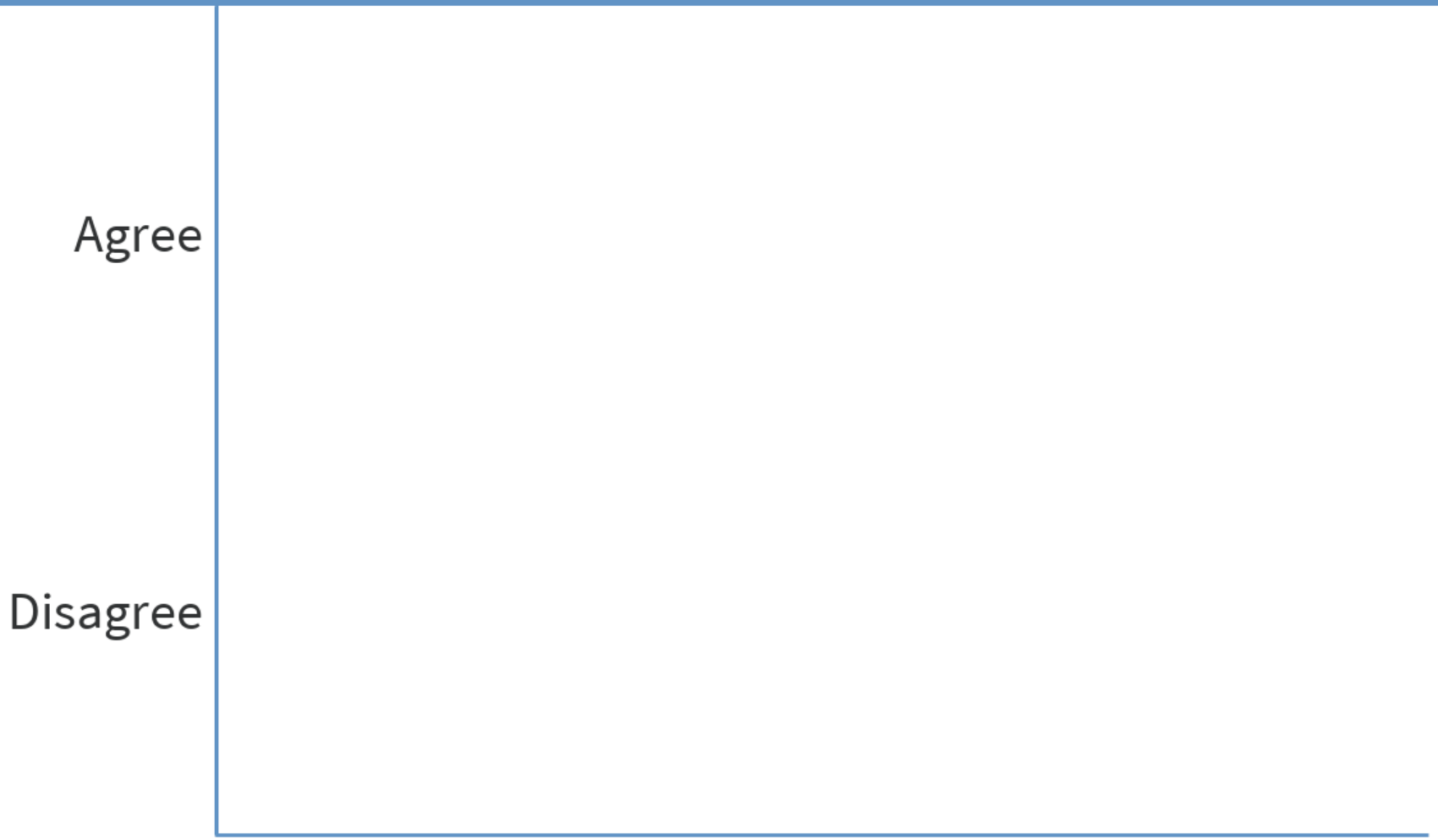



Risk Factors
Age
Sex
Hypertension
Obesity
Diabetes mellitus
Kidney disease
Oxidative stress
Inflammation
Alcohol
Cardiovascular Dysfunction
Atrial stiffness
Cardiac impairments
Remodeling
Elevated natriuretic peptides
RAAS activation
Rheumatic Heart Disease
Mitral valve disease
Rheumatic cardiomyopathy
Atrial Myopathy
Endothelial dysfunction
Premature atrial contractions
Atrial enlargement
Fibrosis
Hemodynamics disturbance
Electrical remodeling
Myocyte dysfunction
Coagulation
Rheumatic
Atrial Fibrillation
EMBOLIC Stroke/TIA
NON-EMBOLIC Stroke/TIA
CARDIO – EMBOLIC Stroke/TIA

Key Point 3 Atrial Myopathy & OAC [comb.]

Signs of atrial myopathy without AF are not sufficient (+evidence) to initiate OAC at present.

Key point #3. Atrial Myopathy & OAC. Signs of atrial myopathy without AF are not sufficient to initiate OAC.



Key Point 2 ESUS Subphenotyping According to Atrial Myopathy

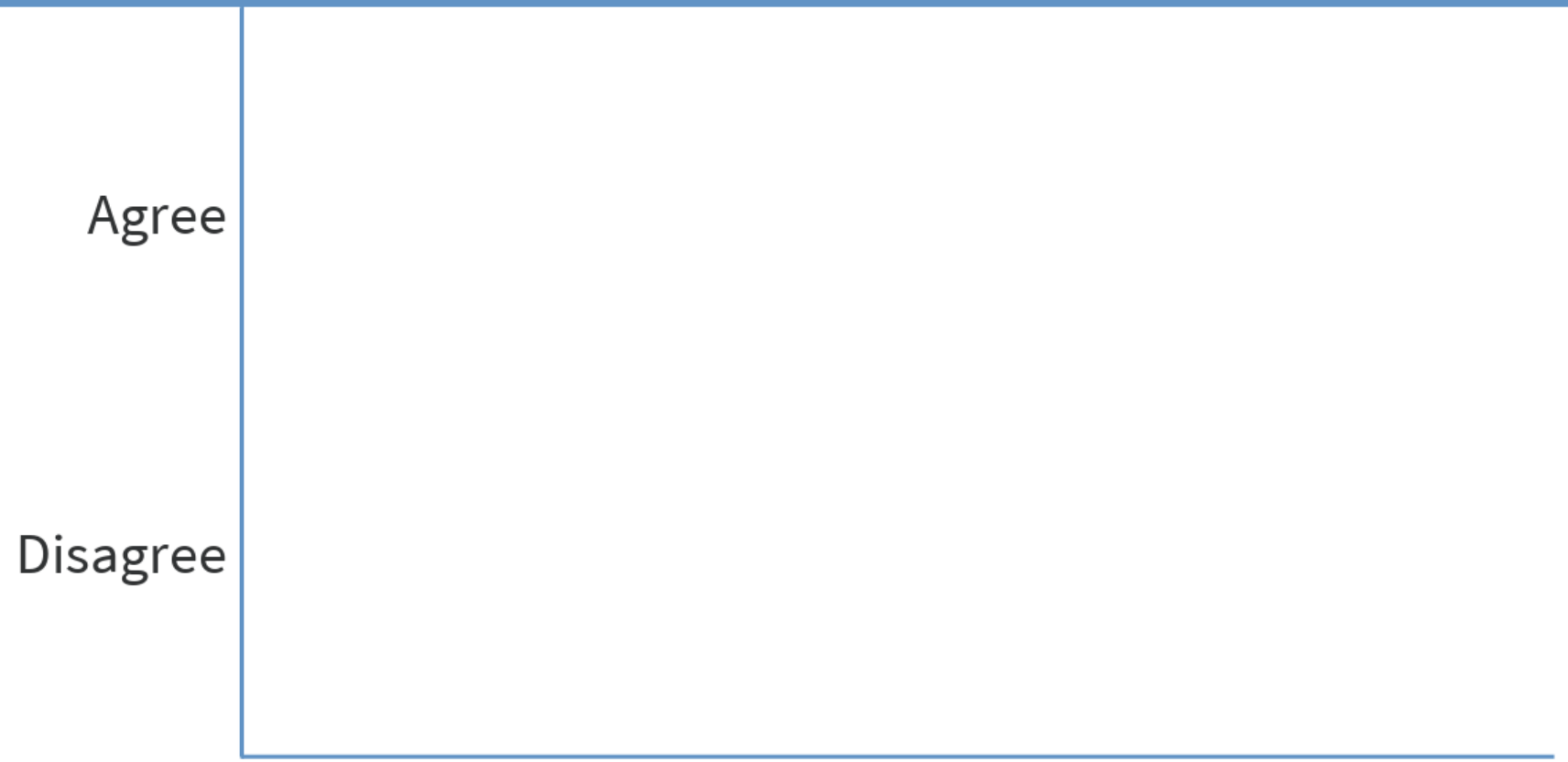
Future stroke classification systems should attempt to phenotype cryptogenic stroke into mechanistically distinct subgroups depending on presence and severity of atrial myopathy.

Rewrite:

In cases of ischemic stroke of uncertain cause should look for evidence of atrial myopathy to inform the intensity/duration of screening for AF.

??

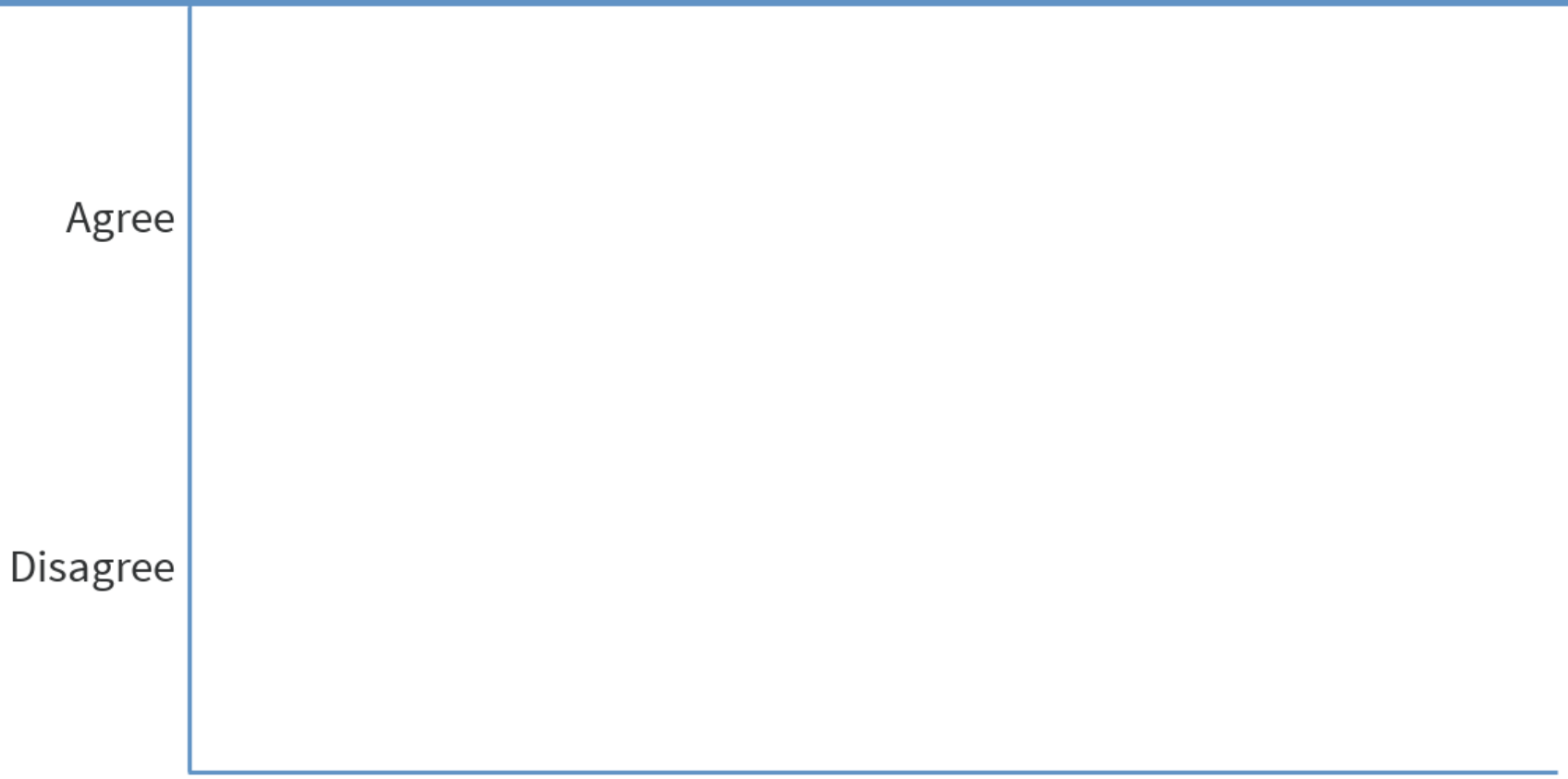
Key point #2. ESUS Subphenotyping according to Atrial Myopathy. Future stroke classification systems should attempt to phenotype ESUS into mechanistically distinct subgroups depending on presence and severity of atrial myopathy.



Key Point 13 AF & Stroke Risk

AF is associated with significantly increased risk of re-current stroke or systemic embolism, in particular in the presence of additional stroke risk factors;
OAC therapy (either well-controlled vitamin K antagonist (VKAs) or NOACs) effectively reduces the risk of ischemic stroke in AF patients and is recommended for new AF detected by ECG screening after stroke.

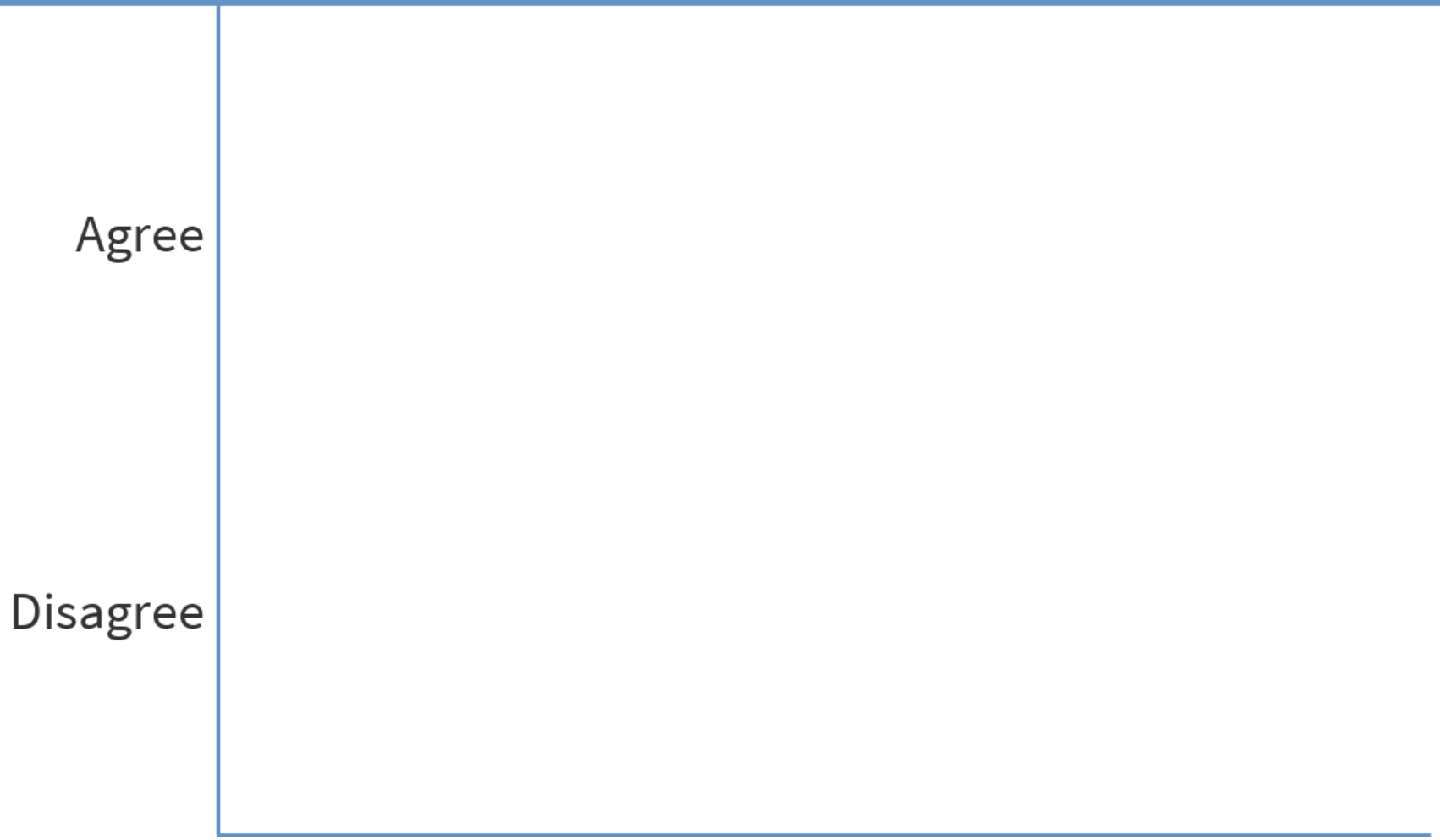
Key point #13. AF & Stroke risk. AF is associated with significantly increased risk of stroke or systemic embolism after stroke, in particular in the presence of additional stroke risk factors; OAC therapy (either well-controlled vitamin K antagonist (VKAs) or NOACs) effectively reduces the risk of stroke in AF patients and is recommended for new AF detected by ECG screening after stroke.



Key Point 5 ESUS & OAC

Fulfilling ESUS criteria is neither an indication for OAC treatment nor for withholding prolonged ECG monitoring.

Key point #5. ESUS and OAC. ESUS alone is not an indication for OAC treatment.



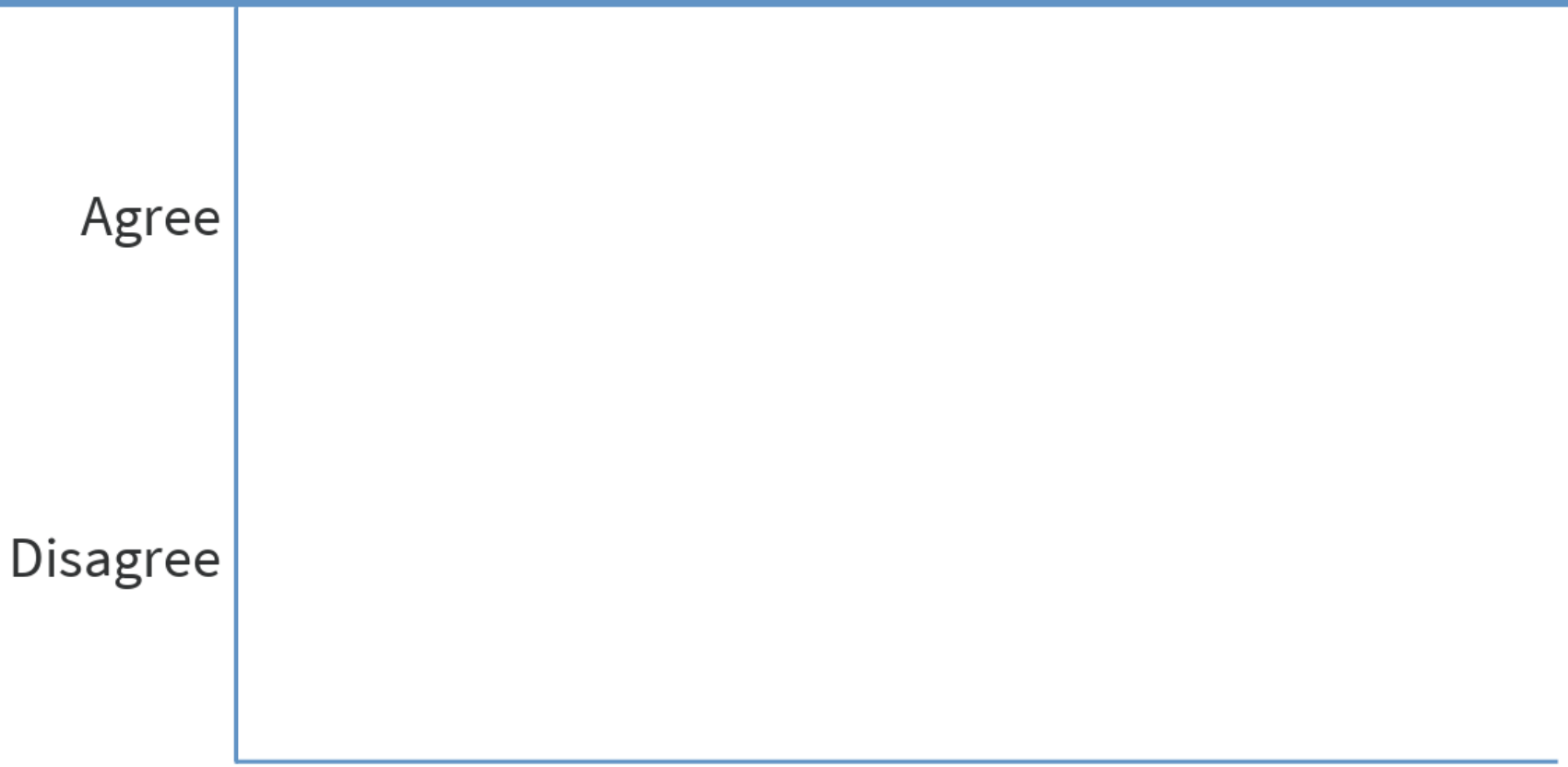
Key Point 7: Clinical Characteristics for Intensified Monitoring [comb.]

Older age and cardiovascular comorbidities, particularly heart failure, may be used to guide selection of more prolonged ECG monitoring for AF.

Table: Risk factors to guide selection of more prolonged ECG monitoring for AF.

- Age
- Heart failure
- Multiple CV comorbidities

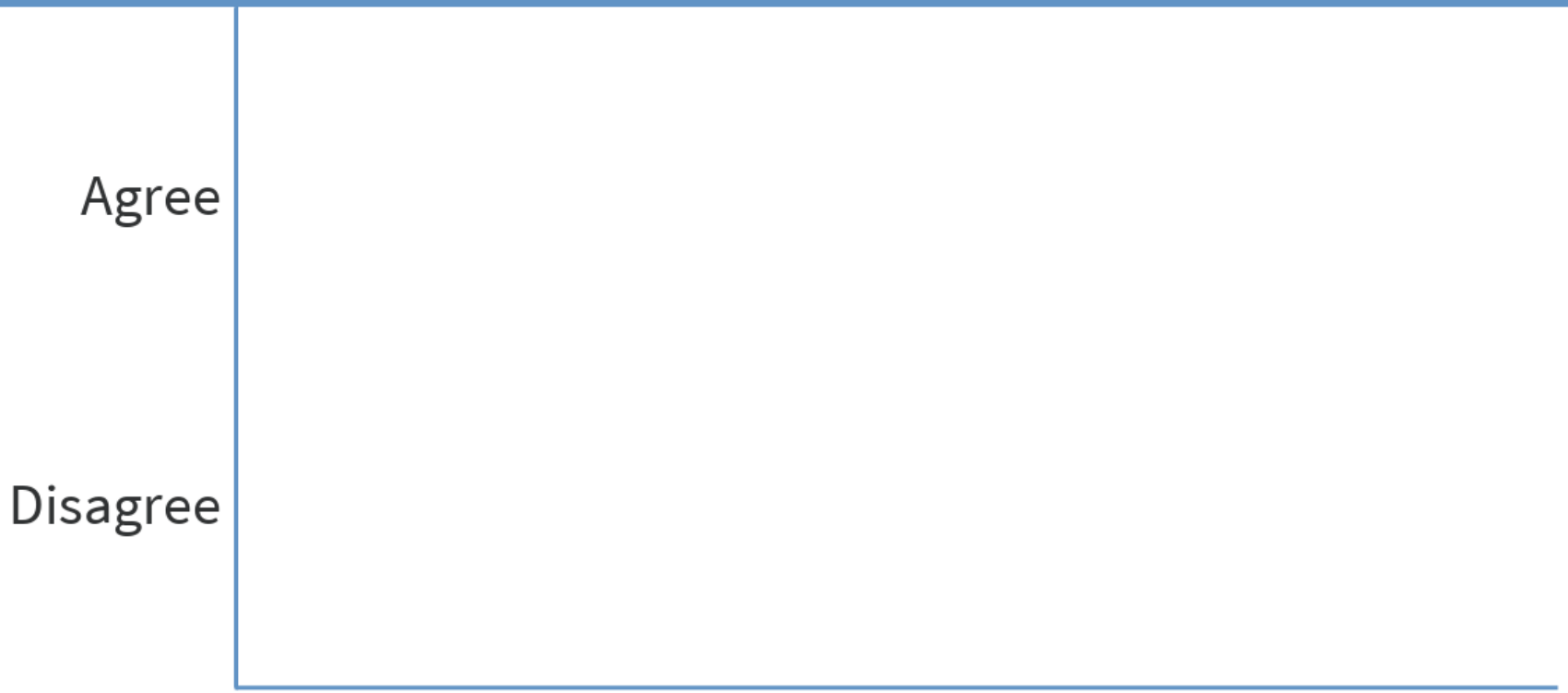
Key point #7. Clinical Characteristics for Intensified Monitoring. Older age and cardiovascular comorbidities, particularly heart failure, may be used to guide selection of more prolonged ECG monitoring for AF.



Key Point 8: Quantifiable Parameters for Atrial Myopathy & Intensified Monitoring [comb.]

Characteristic abnormalities on cardiac imaging or electrocardiography, and biomarkers (particularly natriuretic peptides) suggestive of increased risk of AF (see table…) can be used to guide selection of prolonged ECG monitoring.

Key point #8. Quantifiable Parameters for Atrial Myopathy & Intensified Monitoring. Cardiac imaging, excessive atrial ectopy and biomarkers including natriuretic peptides, suggestive of atrial myopathy, increase yield of AF, and can be used to guide selection of prolonged ECG monitoring for AF.



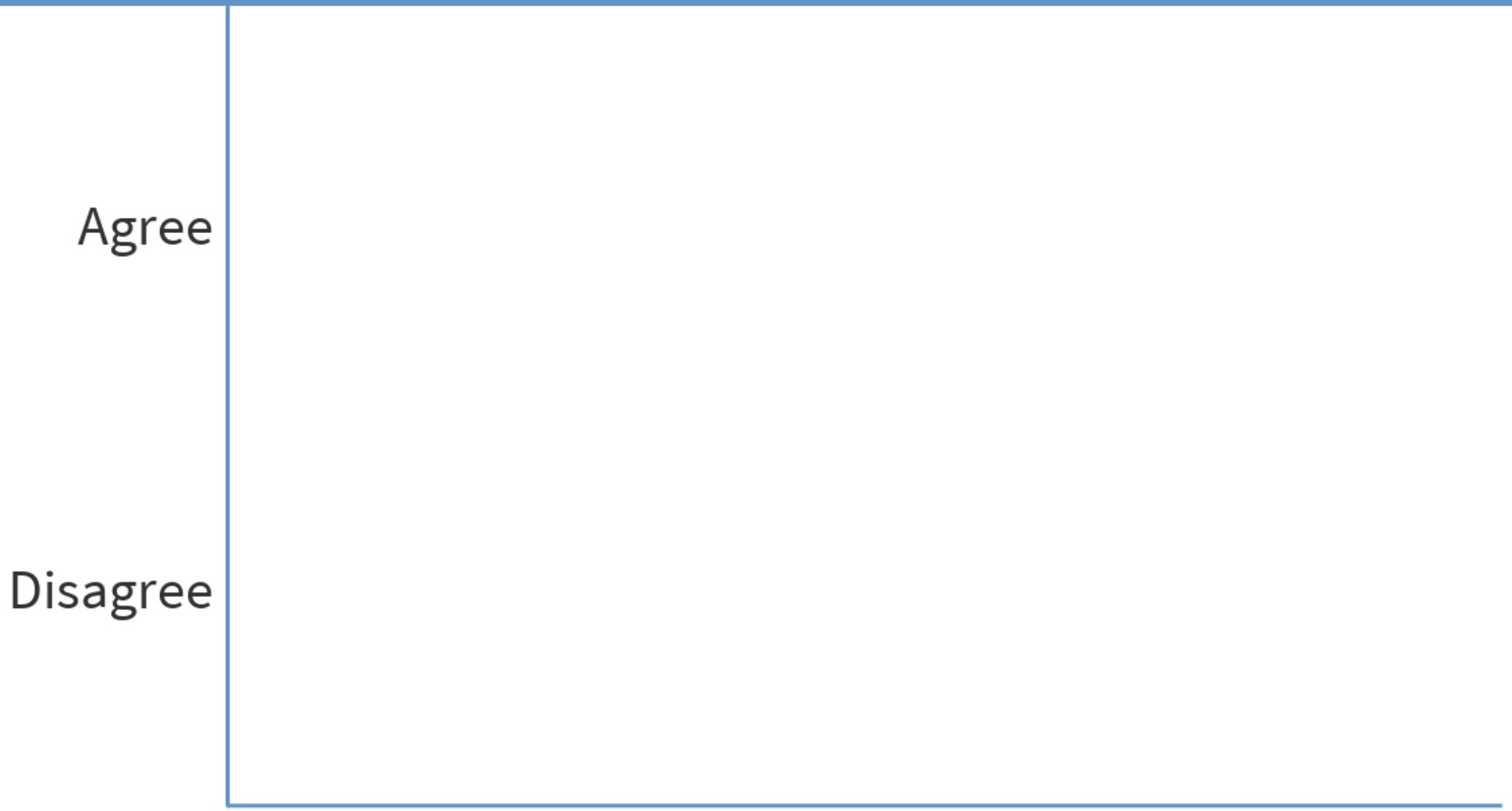
Key Point 9: Brain Imaging [comb.]

Stroke lesion pattern(s) on brain imaging suggestive of embolic source may indicate a need for intensified ECG monitoring for AF.

Comment: Most stroke units would view multi-territory infarcts as strong indication of cardiac source of emboli, therefore, a strong indication for prolonged ECG monitoring.

We need future studies to clarify as to whether stroke morphology on MR does relate to the cause of ischemic stroke.

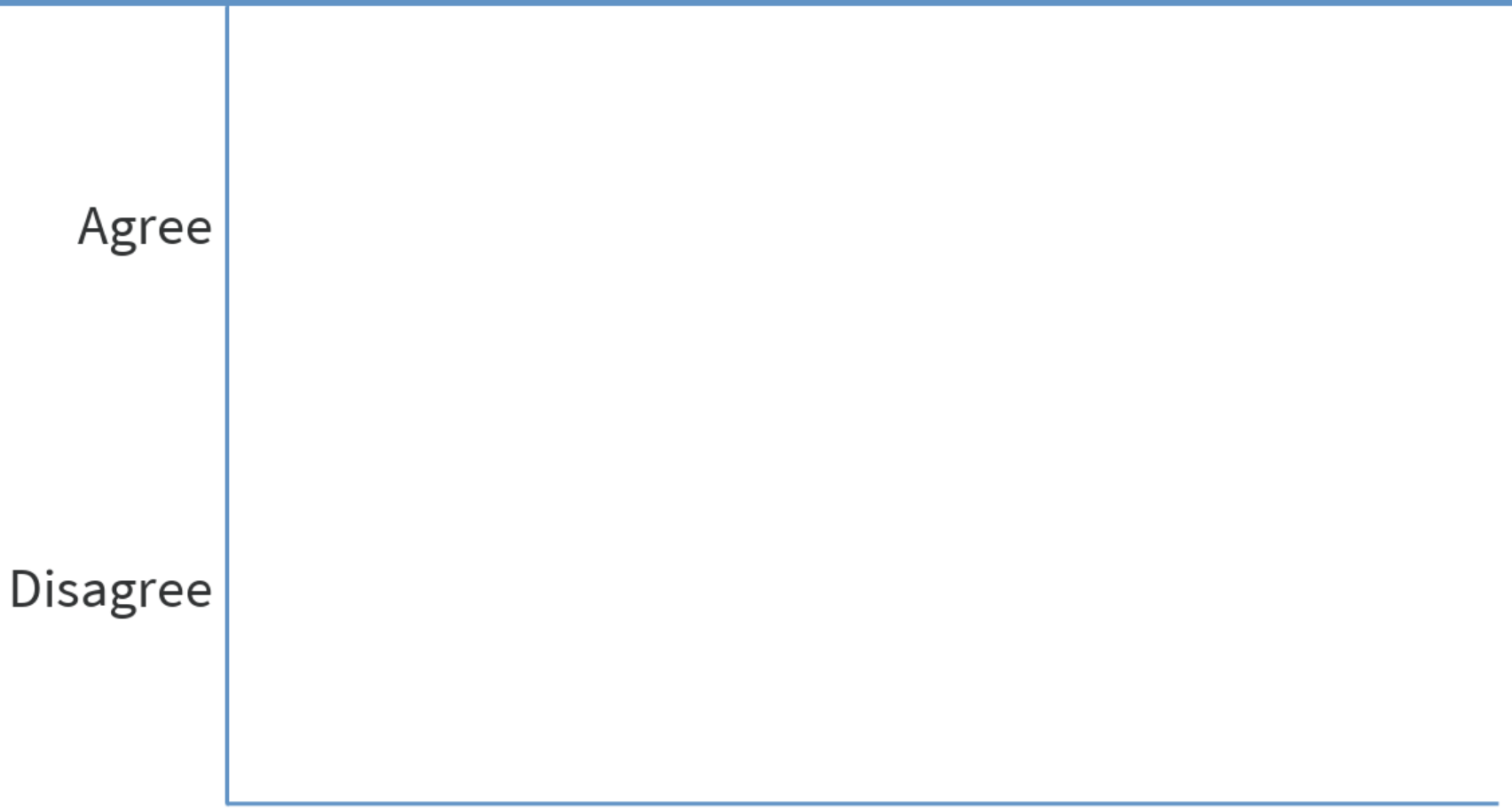
Key point #9. Brain imaging. Brain imaging for stroke lesion pattern(s) should not be used as the sole guide for prolonged ECG monitoring for AF.



Key Point 11 AF Detection Rate

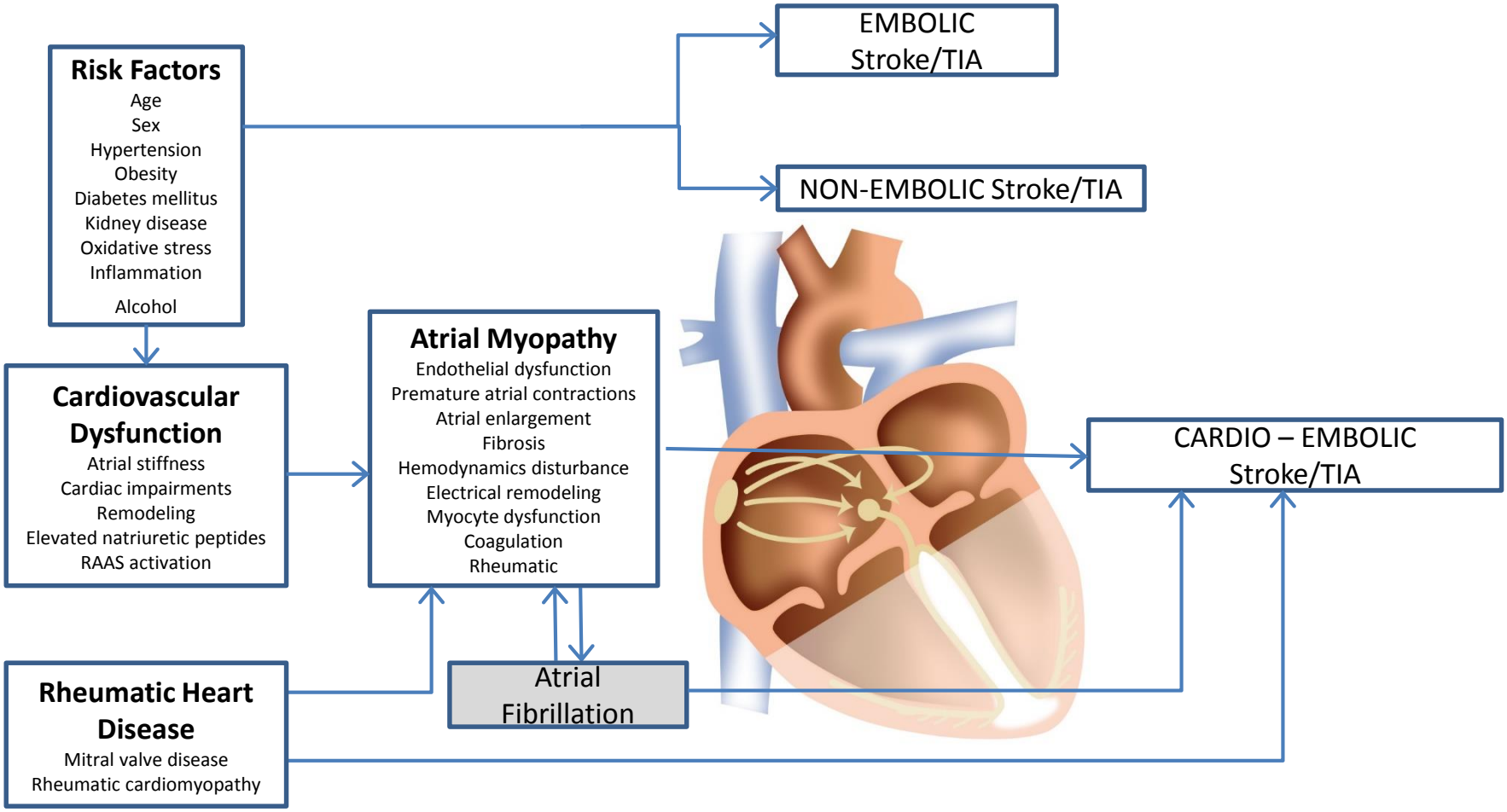
Intensive arrhythmia monitoring strategies result in significantly higher AF detection rates compared to standard monitoring.

Key point #11. AF Detection Rate. Comprehensive arrhythmia monitoring strategies result in significantly higher AF detection rates compared to standard monitoring.



Key Point 3 Atrial Myopathy & OAC

Signs of atrial myopathy without AF are not sufficient to initiate OAC.


Risk Factors
Age
Sex
Hypertension
Obesity
Diabetes mellitus
Kidney disease
Oxidative stress
Inflammation
Alcohol
Cardiovascular Dysfunction
Atrial stiffness
Cardiac impairments
Remodeling
Elevated natriuretic peptides
RAAS activation
Rheumatic Heart Disease
Mitral valve disease
Rheumatic cardiomyopathy
Atrial Myopathy
Endothelial dysfunction
Premature atrial contractions
Atrial enlargement
Fibrosis
Hemodynamics disturbance
Electrical remodeling
Myocyte dysfunction
Coagulation
Rheumatic
Atrial Fibrillation
EMBOLIC Stroke/TIA
NON-EMBOLIC Stroke/TIA
CARDIO – EMBOLIC Stroke/TIA

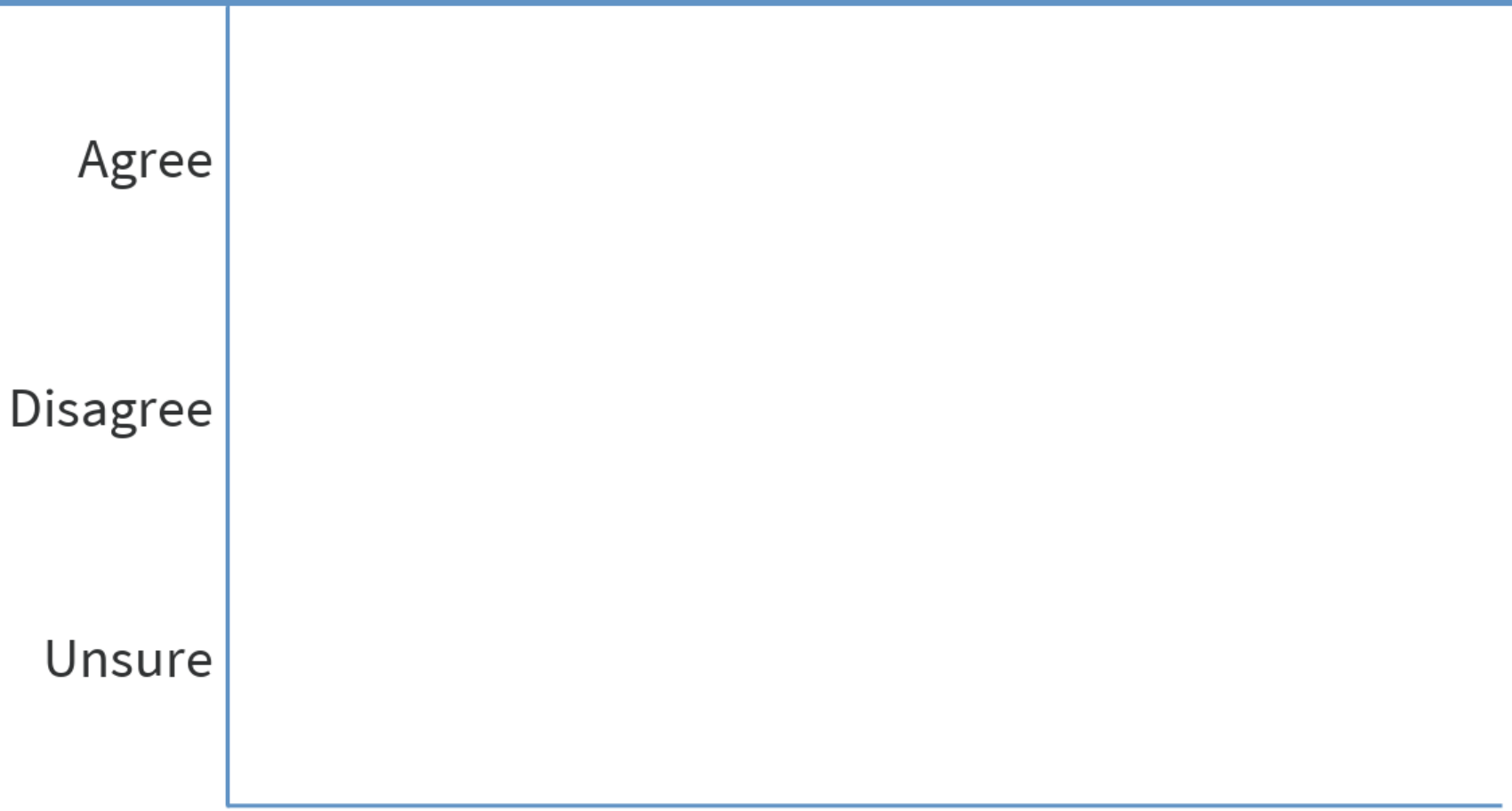
Key Point 4 Diagnosis of AF

The diagnosis of AF requires the documentation by an ECG with sufficient quality to allow confirmation by an experienced physician.

…not a key point – include as a definition.

What kind of ECG? - Any ECG of sufficient quality.
Must be at least 30 sec.

Key point #4. Diagnosis of AF. The diagnosis of AF requires the documentation by an ECG with sufficient quality to allow confirmation by an experienced physician.

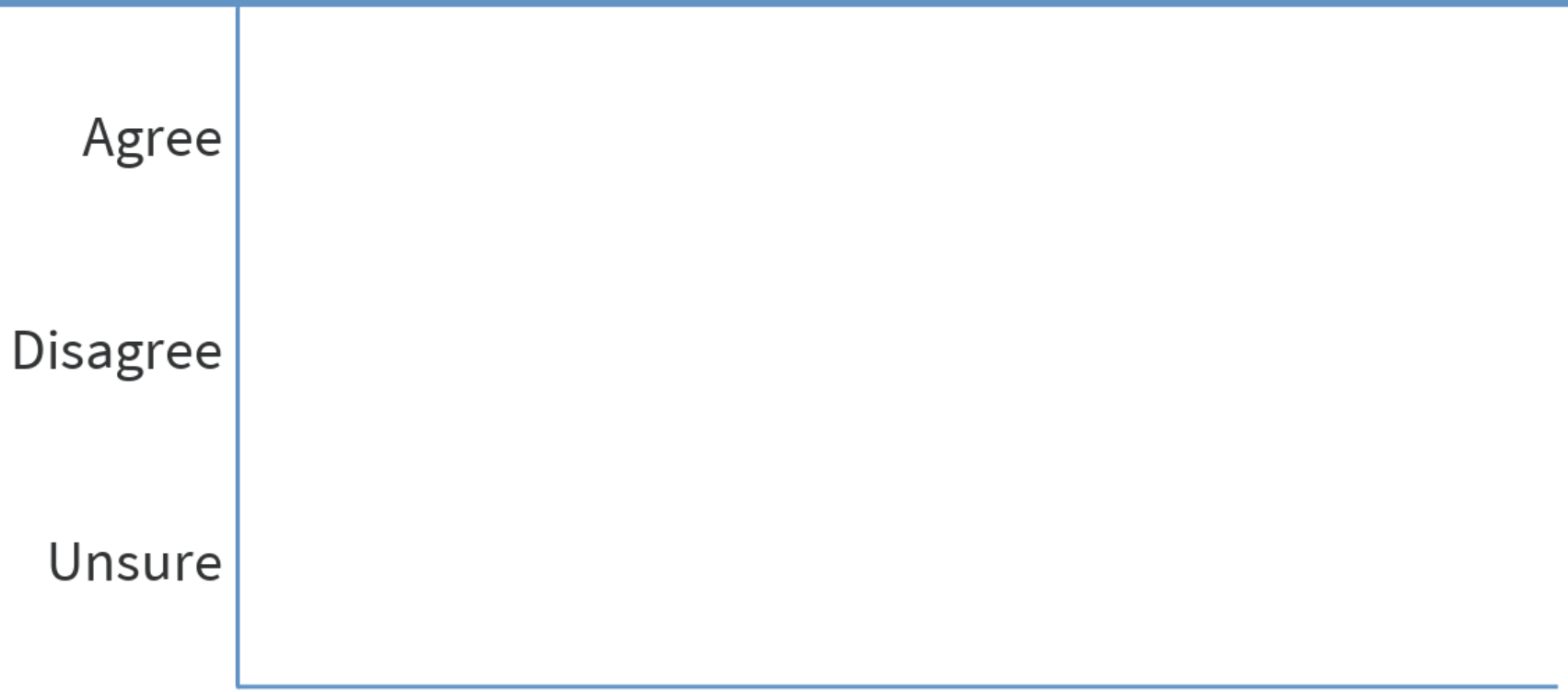


Key Point 4a Length of Episode, Device?

Diagnosis of AF
≥30 sec on ECG, telemetry, Holter recordings or other screening devices based on ECG recordings.

Non-sustained AF (<30 sec) is frequent after ischemic stroke but has not the same clinical relevance.

Key point #4a. Length of Episode, Device? Diagnosis of AF ≥30 sec on ECG, telemetry, Holter recordings or other screening devices based on ECG recordings. Non-sustained AF (<30 sec) is frequent after ischemic stroke but has not the same clinical relevance.



Key Point Minimum AF Duration

- AF of any duration
- ≥30 sec on ECG, telemetry, Holter recordings or other screening devices based on ECG recordings.
- 30 sec to 5 min
- ≥5 min to 24 h

Comment: AF > 30 seconds is not correlated with outcomes. Minimum duration is likely different between monitoring strategies.

Key Point. Minimum AF Duration:

AF of any duration

≥30 sec on ECG, telemetry, Holter recordings or other screening devices based on ECG recordings

30 sec to 5 min

≥5 min to 24 h

Key Point Definition AF Burden

-Pattern
-Burden

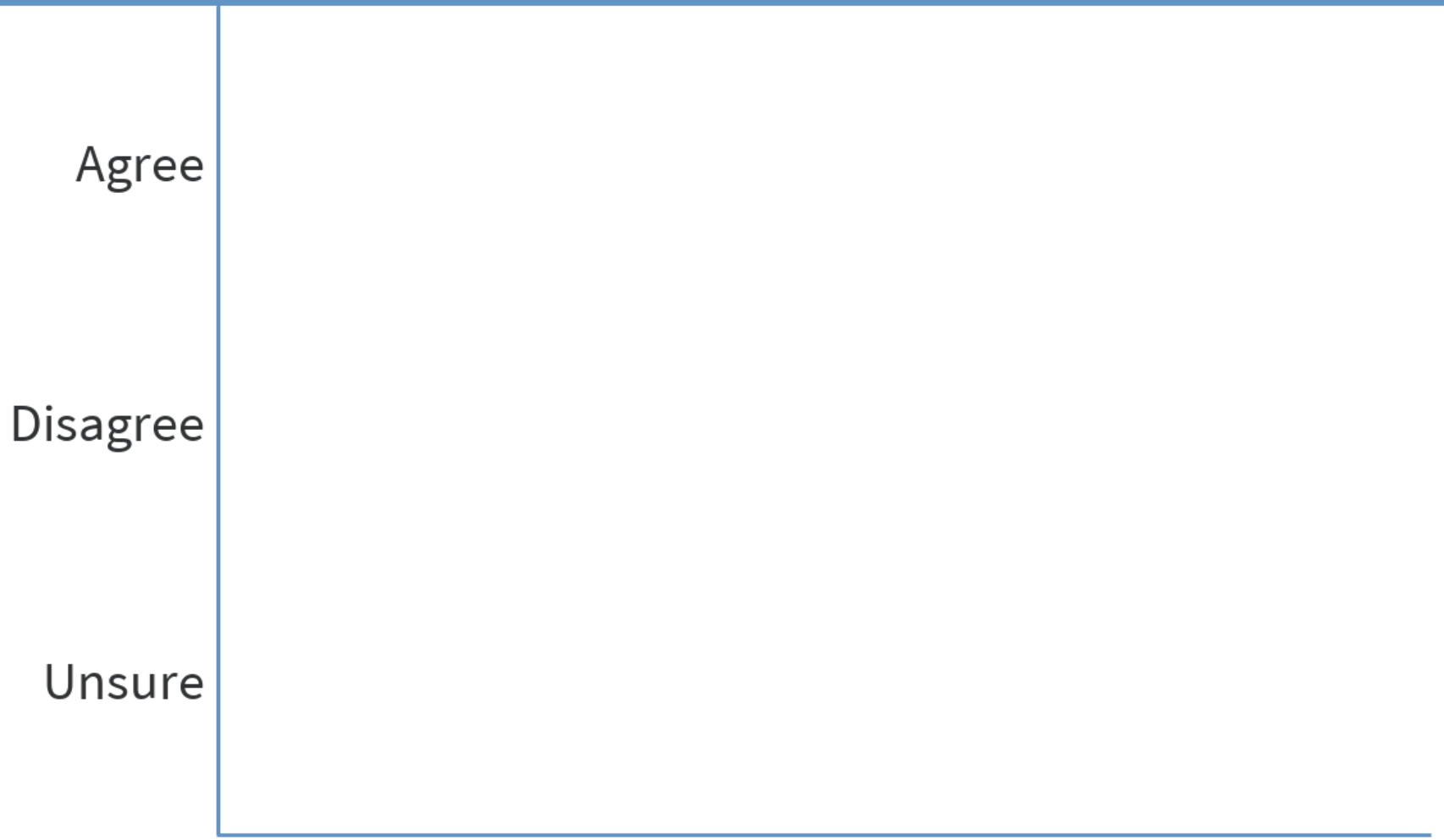
- Longest duration
- Number of AF episodes during a monitoring period
- Proportion of time an individual is in AF during a monitoring period (expressed as a percentage)

This is an area of uncertainty, even more so post-stroke.

Key Point Definition AF Burden

There is a threshold for stroke risk.

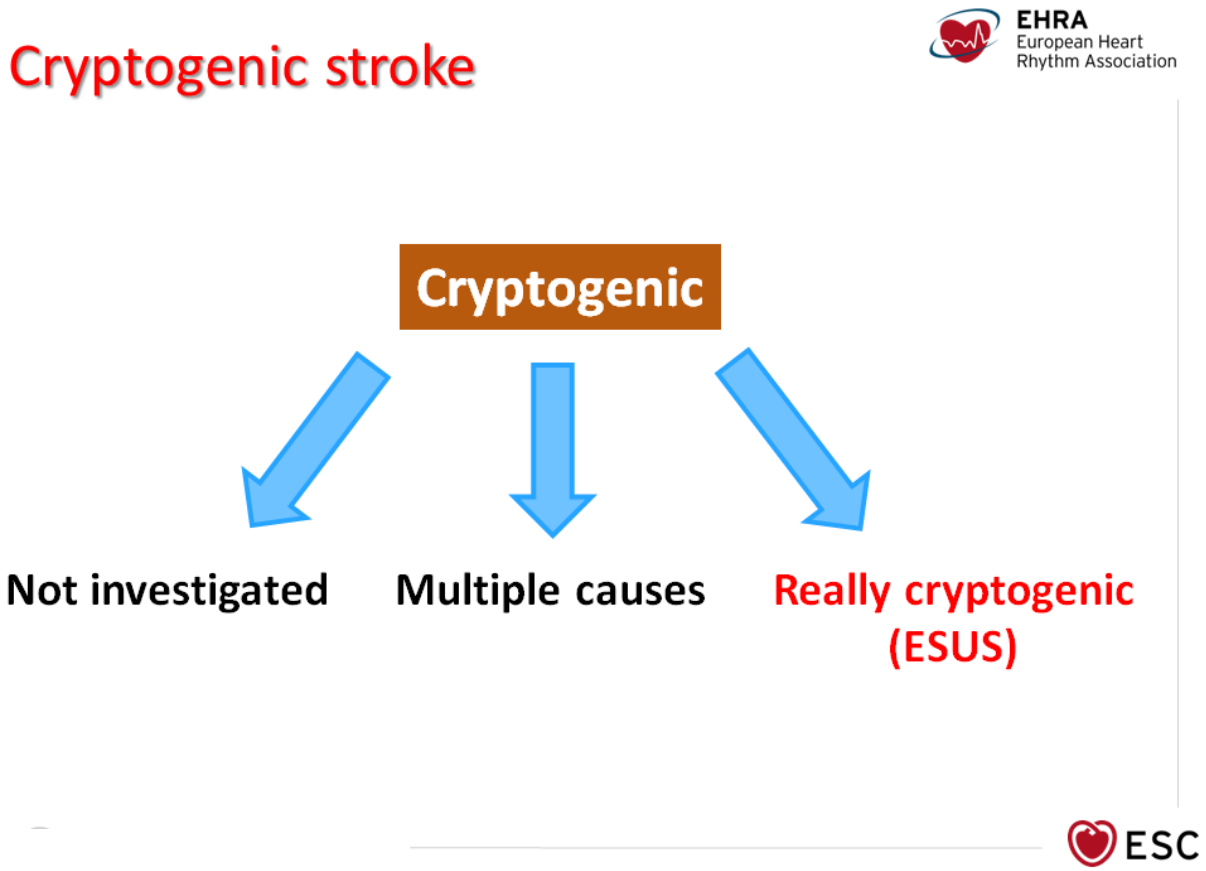
Key point. Definition of AF Burden. There is a threshold for stroke risk.



Definition Cryptogenic Stroke & ESUS

The term cryptogenic stroke is used to describe patients with ischemic stroke for whom the etiology of stroke is unclear. It is a heterogeneous term which includes three distinct subgroups of patients: a) those cases in whom the cause of stroke was not identified because the proper diagnostic investigation was not performed or was incomplete, b) those cases in whom multiple causes of stroke were identified and c) those cases in whom the cause of stroke was not identified despite the recommended diagnostic work-up. The term Embolic stroke of undetermined source (ESUS) is used to describe the latter cases, and should be preferred over the term cryptogenic stroke.

Definition Cryptogenic Stroke & ESUS



Slide provided by George Ntaios

Key Point 5 ESUS & OAC

ESUS alone is not an indication for OAC treatment.

Key Point 6: 24 hour Holter in Cryptogenic Stroke

All patients with ischemic stroke of unknown cause (cryptogenic stroke or ESUS) require a 24 hour Holter monitor.

Key Point 7: Clinical Characteristics for Intensified Monitoring

Older age and cardiovascular comorbidities, particularly heart failure, may be used to guide selection of more prolonged ECG monitoring for AF.

Key Point 8: Quantifiable Parameters for Atrial Myopathy & Intensified Monitoring

Cardiac imaging, excessive atrial ectopy and biomarkers including natriuretic peptides, suggestive of atrial myopathy, increase yield of AF, and can be used to guide selection of prolonged ECG monitoring for AF.

Key Point 9: Brain Imaging

Brain imaging for stroke lesion pattern(s) should not be used as the sole guide for prolonged ECG monitoring for AF.

Comment: Most stroke units would view multi-territory infarcts as strong indication of cardiac source of emboli, therefore, a strong indication for prolonged ECG monitoring.

We need future studies to clarify as to whether stroke morphology on MR does relate to the cause of ischemic stroke.

Key Point 10 AF Detection Rate

The AF detection rate after cryptogenic stroke is a function of length of monitoring, the definition of what duration of AF constitutes an episode, the interval from the index stroke to the start of monitoring, the type of stroke, and patient selection.

Key Point 11 AF Detection Rate

Comprehensive arrhythmia monitoring strategies result in significantly higher AF detection rates compared to standard monitoring.

Key Point 12 AF Burden & Stroke Risk

After stroke, there is likely to be a relationship between AF burden/load on continuous AF monitoring and thromboembolic risk.

Key Point 13 AF & Stroke Risk

AF is associated with significantly increased risk of stroke or systemic embolism after stroke, in particular in the presence of additional stroke risk factors;
OAC therapy (either well-controlled vitamin K antagonist (VKAs) or NOACs) effectively reduces the risk of stroke in AF patients and is recommended for new AF detected by ECG screening after stroke.

Key Point 14 NOACs in Post Stroke AF OAC

NOACs may provide a greater absolute benefit than VKAs in patients with AF and prior stroke/TIA compared to those without prior stroke/TIA.

Key Point 15 Harms of AF Screening

As with all screening procedures, potential harm may arise from over-diagnosis and over-treatment that lead to worries at the screened patient level and waste of valuable healthcare resources. For post-stroke AF screening, risks are more circumscribed and can be counter-balanced by standardization, continuous quality control of the screening process and generation of further evidence. Benefits of screening very likely outweigh potential harm.

Key Point 16 Cost-Effectiveness

Screening for AF following stroke has consistently been found to be cost-effective.

Key Point 17 Screening Modality Recommendation

There is no consensus as to most effective screening modality or duration and optimal cost-benefit ratio.

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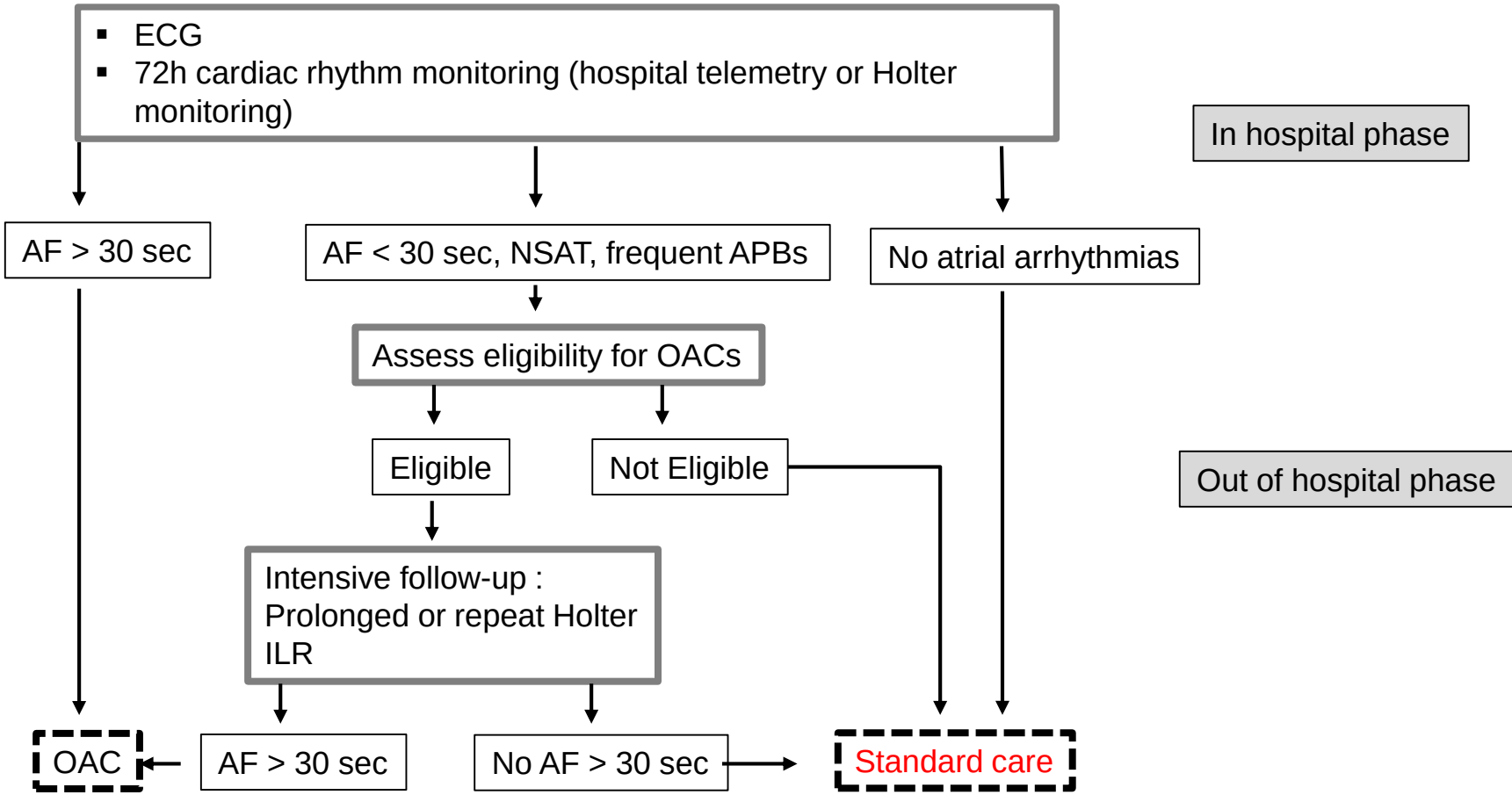
Intensified AF screening in ~~non-lacunar~~, ischemic stroke ~~after exclusion of great artery disease~~

A)



Unless contraindicated for another reason

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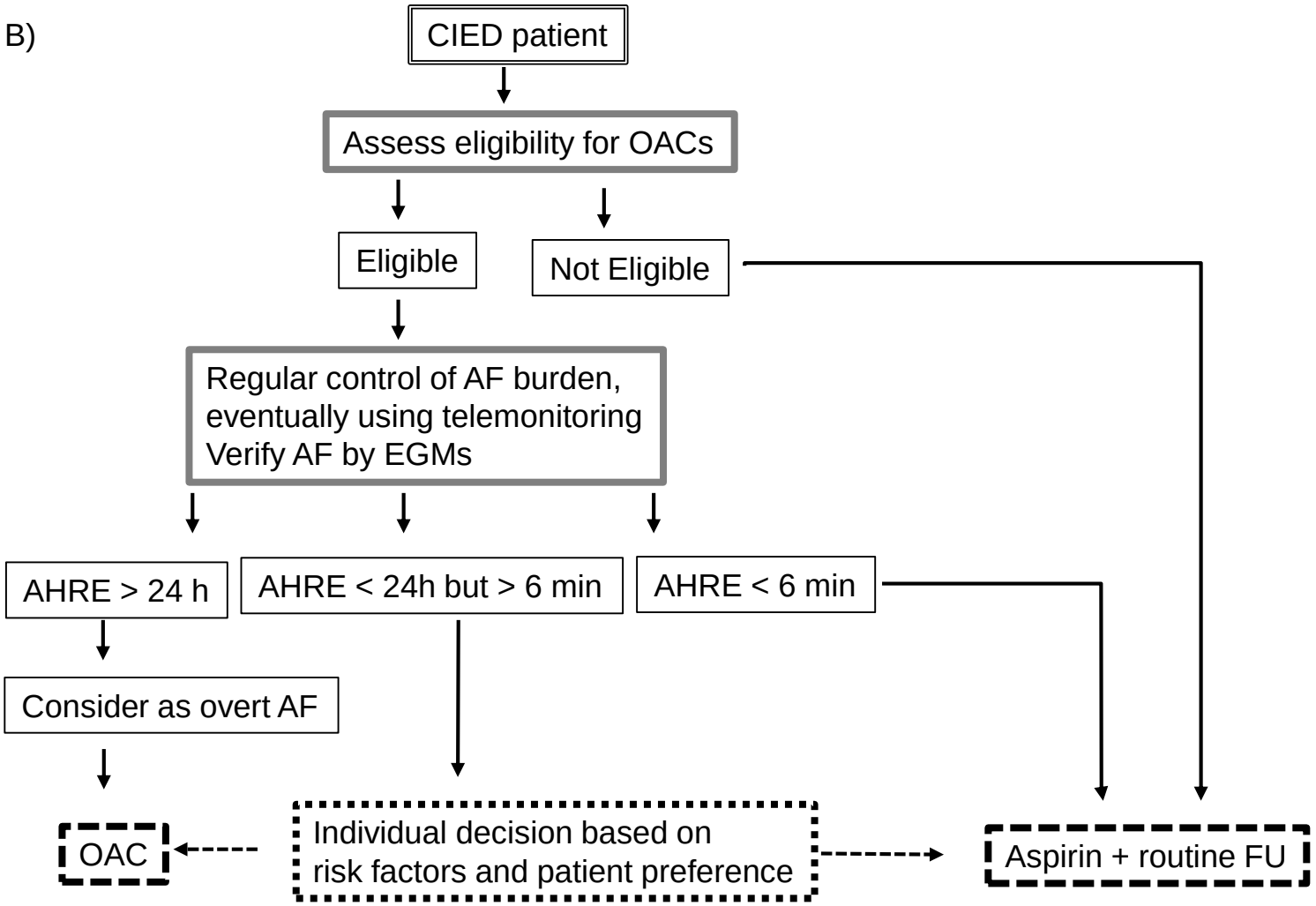
Intensified AF screening in non-lacunar, ischemic stroke after exclusion of great artery disease in CIED carriers

B)



Key Point 18 Current Guidelines

Guidelines recommend AF screening in ischemic stroke patients, but remain inconsistent about the selection of patients for screening and vague on the methods and duration of screening in specific patients.

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SEVENTH FRAMEWORK PROGRAMME

Bundesministerium für Bildung und Forschung

Additional Points for Discussion

- Whether to include Leif Friberg‘s table
- Difference in treatment symptomatic vs. asymptomatic AF?

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First Ever Diagnosis of AF within 14 Days of Ischemic Stroke (Predictors of underlying AF)

			With AF		Univariate	Multivariable
		All	n	%	OR (95% CI)	OR (95% CI)
Sex	Male	40,088	6,344	15.8%	reference	reference
	Female	35,925	7,014	19.5%	1.29 (1.24-1.34)	1.03 (0.99-1.08)
Age, years	<60	8,156	410	5.0%	reference	reference
	60-69	14,315	1,478	10.3%	2.18 (1.94-2.44)	2.07 (1.84-2.34)
	70-79	22,181	3,680	16.6%	3.76 (3.38-4.18)	3.26 (2.91-3.65)
	80-89	25,666	6,099	23.8%	5.89 (5.31-6.53)	4.86 (4.35-5.43)
	90+	5,695	1,691	29.7%	7.98 (7.12-8.95)	6.53 (5.77-7.40)
Myocardial infarction	Yes	6,502	1,287	19.8%	1.17 (1.10-1.25)	0.96 (0.89-1.04)
	No	69,511	12,071	17.4%	reference	reference
Heart failure	Yes	5,477	1,345	24.6%	1.59 (1.49-1.69)	1.27 (1.18-1.38)
	No	70,536	12,013	17.0%	reference	reference
Mitral stenosis	Yes	46	13	28.3%	1.85 (0.97-3.51)	1.54 (0.75-3.18)
	No	75,967	13,345	17.6%	reference	reference
Other valvular disease	Yes	1,485	400	26.9%	1.75 (1.56-1.97)	1.43 (1.26-1.63)
	No	74,528	12,958	17.4%	reference	reference
Hypertension	Yes	44,485	8,789	19.8%	1.45 (1.40-1.51)	1.31 (1.26-1.37)
	No	31,528	4,569	14.5%	reference	reference
Stroke/TIA/ systemic embolism	Yes	14,205	2,570	18.1%	1.04 (1.00-1.10)	0.93 (0.88-0.98)
	No	61,808	10,788	17.5%	reference	reference
Haemorrhagic stroke	Yes	858	101	11.8%	0.62 (0.51-0.77)	0.64 (0.51-0.82)
	No	75,155	13,257	17.6%	reference	reference
Any bleeding	Yes	8,363	1,451	17.4%	0.98 (0.93-1.04)	0.89 (0.83-0.95)
	No	67,650	11,907	17.6%	reference	reference
Diabetes	Yes	15,916	2,689	16.9%	0.94 (0.90-0.99)	0.90 (0.85-0.94)
	No	60,097	10,669	17.8%	reference	reference
Renal failure	Yes	1,488	259	17.4%	0.99 (0.86-1.13)	0.87 (0.74-1.02)
	No	74,525	13,099	17.6%	reference	reference
Liver disease	Yes	459	64	13.9%	0.76 (0.58-0.99)	1.02 (0.75-1.38)
	No	75,554	13,294	17.6%	reference	reference
Thyroid disease	Yes	2,158	367	17.0%	0.96 (0.86-1.08)	0.77 (0.68-0.87)
	No	73,855	12,991	17.6%	reference	reference
Chronic obstructive pulmonary disease	Yes	2,400	358	14.9%	0.82 (0.73-0.92)	0.79 (0.70-0.90)
	No	73,613	13,000	17.7%	reference	reference
Cancer within 3 years	Yes	3,348	519	15.5%	0.85 (0.78-0.94)	0.82 (0.74-0.91)
	No	72,665	12,839	17.7%	reference	reference
Dementia	Yes	623	421	67.6%	10.06 (8.50-11.91)	7.58 (6.30-9.12)
	No	75,390	12,937	17.2%	reference	reference
Smoker, current or stopped < 3 months*	Yes	11,860	1,166	9.8%	0.48 (0.45-0.51)	0.75 (0.70-0.80)
	No	57,084	10,625	18.6%	reference	reference
Alcohol index§	Yes	1,642	142	8.7%	0.44 (0.39-0,52)	0.78 (0.64-0.95)
	No	74,371	13,216	17.8%	reference	reference
Age≥75 years + heart failure	Yes	4,163	1,120	26.9%	1.79 (1.67-1.93)	n/a
	No	71,850	12,238	17.0%	reference	
CHA_2DS_2-VASc ≥ 5 points	Yes	14,802	3,333	22.5%	1.48 (1.42-1.55)	n/a
	No	61,211	10,025	16.4%	reference	
	All	76,013	13,358	17.6%		

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First Ever Diagnosis of AF within 14 Days of Ischemic Stroke
Predictors of unterlying AF

Predictors for underlying AF among patients with ischaemic stroke
(ICD-10 code I63)

First ever diagnosis of AF made within 14 days after admittance for ischaemic stroke

*Information about smoking status was not available for 9,350 patients (9.9% of all). §"Alcohol index" is a set of diagnostic codes used by the Swedish Board of Health and Welfare for annual reporting of alcohol related mortality (ICD-10 codes E244,F10,G312,G621, G721, I426, K292, K70, K860, O35,P043,Q860,T51,Y90-91,Z502,Z714).
In the multivariate analysis all cofactors in the table were included as covariates

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AF Detection Rates in CRYSTAL AF Study At 6, 12, and 36 Months after Cryptogenic Stroke

Fig 2

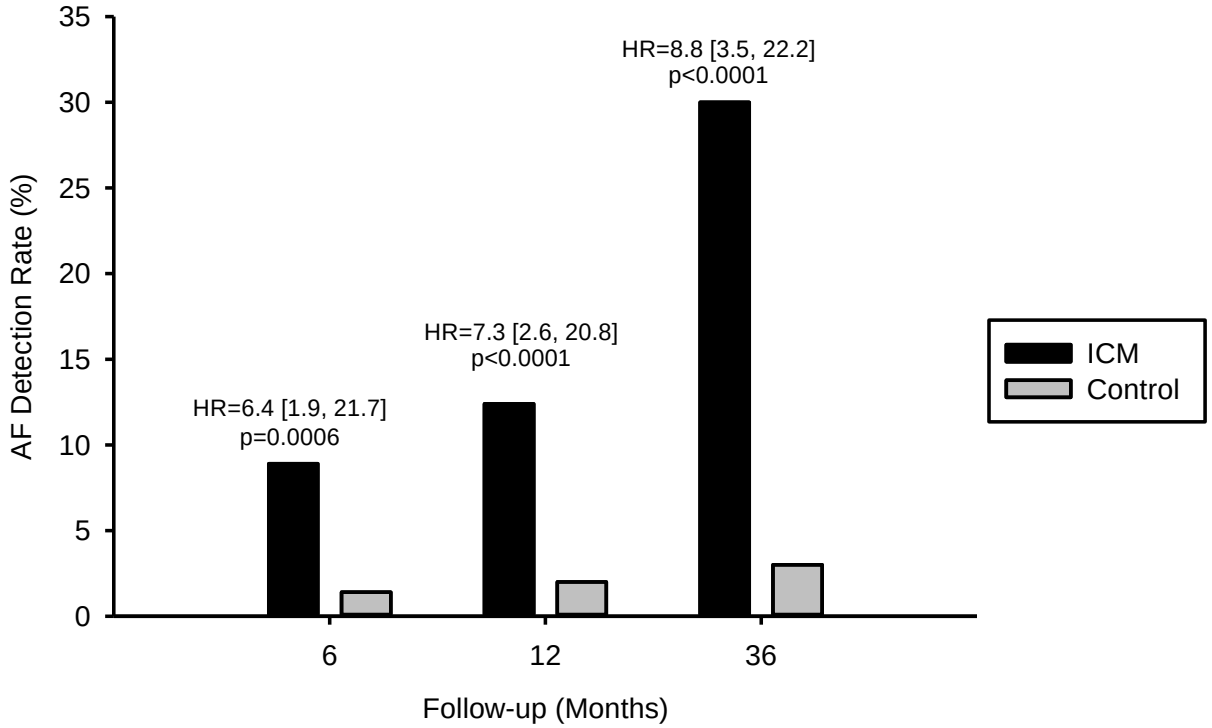

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Table 1. Detection of new AF in post-stroke subjects, by screening method

	No. of Patients	Screening method	Study population	Percent AF	Type of study
Screening with resting ECG					
Bansil et al 2004[1]	121	ECG at admission	Ischemic stroke	5	Consecutive clinical cases
Jabaudon et al 2004[2]	149	Serial ECG	Ischemic stroke/TIA	6.7	Consecutive clinical cases
Kallmünzer et al 2009[3]	271	ECG at admission	Ischemic stroke	9.6	Consecutive clinical cases
Stahrenberg et al 2010[4]	281	ECG at admission	Ischemic stroke/TIA	15.7	RCT
Gumbinger et al 2012[5]	312	ECG at admission	Ischemic stroke/TIA	8.4	Clinical cases
Screening with Holter ECG					
Tonet et al 1981[6]	100	18-54h ECG	Stroke/TIA of suspected embolic origin	1	Clinical cases
Kessler et al, 1995[7]	93	24hECG	Ischemic stroke	1	Prospective consecutive clinical sample
Schuchert et al, 1999[8]	82	72hECG	Ischemic stroke	6	Consecutive clinical cases
Jabaudon et al 2004[2]	139	24hECG	Ischemic stroke/TIA	5	Consecutive clinical cases
Gunalp et al, 2006[9]	26	24ECG	Thromboembolic cryptogenic stroke	42.3	Clinical cases
Stahrenberg et al 2010[4]	224	7 days	Ischemic stroke/TIA	12.5	Consecutive clinical cases
Dangayach et al 2011[10]	51	48hECG x 2	Cryptogenic stroke	29	Clinical cases
Rizos et al 2012[11]	496	NA	Ischemic stroke/TIA	2.8	Consecutive clinical cases
Wachter et al 2017[12]	200	Repeated 24hECGs at 0, 3 and 6 months	Ischemic stroke	14	Randomized observational

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Table 1. Detection of new AF in post-stroke subjects, by screening method

	No. of Patients	Screening method	Study population	Percent AF	Type of study
Inpatient Telemetry monitoring					
Bansil et al, 2004[1]	121	48h	Ischemic stroke	5	Consecutive clinical cases
Vivanco Hidalgo 2009[13]	465	55h (SD 36h)	Ischemic stroke/TIA	7	Clinical cases
Rizos et al 2010[14]	136	NA – duration of care at ward	Ischemic stroke/TIA	21	Prospective clinical cases
Gumbinger et al 2012[5]	281		Ischemic stroke/TIA	4.6	Clinical cases
Kallmünzer et al 2012[3]	271	NA	Ischemic stroke	7	
Rizos et al 2012[11]	496	NA	Ischemic stroke/TIA	5.4[b]	Consecutive clinical cases
Grond et al 2013[15]	1135	72h	Stroke/TIA	4.3	Prospective multicentre cohort
Wachter et al 2017[16]	198	24h	Ischemic stroke	5	Randomized observational
Pagola et al 2018[17]	146	28 days, wearable textile Holter	Cryptogenic stroke	22	RCT
Event recorder					
Barthelemy et al 2003[18]	28	96h	Stroke or TIA	14	Consecutive clinical cases
Jabaudon et al 2004[2]	88	7 days	Ischemic stroke/TIA	5.7	Consecutive clinical cases
Wallman et al 2007[19]	127	7 days	Ischemic stroke	14	Clinical cases
Flint et al 2012	239	30 days	Cryptogenic stroke	11	Prospective multicentre registry
Hornig et al 2012		?			?
Gladstone et al 2014	280	30 days	Cryptogenic stroke	16	RCT
Implantable devices					
Sanna et al 2014	221	6 months	Cryptogenic stroke, 24hECG negative	9	RCT
Ziegler et al 2017	1247	2 years	Cryptogenic stroke	21.5	Registry
Seow et al 2018	71	12 mo	Cryptogenic stroke	15.2	

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Table 3. Temporal relationship of device-detected AF and thromboembolic events

Year	Trial	Number of patients with TE Event	Definition of AF episode	Any AF Detected Prior to TE Event	AF Detected only after TE Event	No AF in 30 Days Prior to TE Event	Any AF in 30 Days Prior to TE Event
2011	TRENDS	40	5 minutes	20/40 (50%)	6/40 (15%)	29/40 (73%)	11/40 (27%)
2012	ANGELS	33	5 minutes	21/33 (64%)	NA	22/33 (77%)	11/33 (33%)
2014	ASSERT	51	6 minutes	18/51 (35%)	8/51 (16%)	47/51 (92%)	4/51 (8%)
2014	IMPACT	69	36/48 atrial beats ≥200bpm	20/69 (29%)	9/69 (13%)	65/69 (94%)	4/69 (6%)

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Table 4. AF Detected by Outpatient Cardiac Monitoring in Cryptogenic Stroke

Study	No. Patients	AF Definition	Monitoring Type and Duration	AF Detection Yield	Notes
Tayal et al.[18] 2008	56	Any Duration	MCOT-21 days	Overall: 23% • AF<30 seconds: 18% • AF>30 seconds: 5%	Time to detection: Median=7 days Range=2–19 days
Elijovich et al.[19] 2009	20	Not defined	Event Monitor-30 days	20%	
Gaillard et al.[20] 2010	98	32 seconds	TTM-30 days	9%	
Bhatt et al.[21] 2011	62	30 seconds	MCOT-28 days	24% using AF duration of 5 minutes, yield was 9%	93% of PAF was detected within first 21 days Median duration of monitoring: 21 days (range 2–28)
Flint et al.[22] 2012	236	5 seconds	MCOT-30 days	Overall: 11% • AF<30 seconds: 4% • AF>30 seconds: 7%	
Kamel et al.[23] 2013	20	30 seconds	MCOT-21 days	0%	Only 64% wore the monitor for the duration
Miller et al.[24] 2013	156	30 seconds	MCOT-30 days	Overall: 17% • AF<30 seconds: 12% • AF>30 seconds: 4%	Only 62% completed 21 days
EMBRACE; Gladstone et al.[12] 2014	572	30 seconds 2.5 minutes	Event Monitor-30 days vs. 24 hr Holter	16.1% (45/280) event monitor 3.2% (9/277) 24hr Holter at 90 days 9.9% (28/284) event monitor 2.5% (7/277) 24hr Holter at 90 days	

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Table 5. AF detected by insertable cardiac monitors in cryptogenic stroke

Study	# Patients	AF Definition	Monitoring Duration	AF Detection Yield	Notes
Cotter et al.[25] 2013	51	2 minutes	For AF detection: 48 (0–154) days For those with NO AF detected. Mean 229 (116) days	25.5%	median duration of recording prior to first episode of AF was 48 days (IQR 34–118; range 0–154) median duration of first detected AF=6 (range 1–4,320) minutes
Ritter et al.[26] 2013	60	2 minutes	64 days (1-556) after implant	16.7%	7 day Holter detected AF in only 1.7%
Etgen et al.[27] 2013	22	6 minutes	time to first new AF was on average 5 months after stroke	27.3%	
Rojo-Martinez et al.[28] 2013	101	2 minutes	281±212 days	33.7%	
SURPRISE[29] 2014	85	2 minutes	569±310 days 18 months	16.1 %	mean time from stroke onset to first AF episode using ICM=109±48 days
CRYSTAL AF[11] 2014	221	>30 seconds*		8.9% at 6 months 12.4% at 12 months 30.0% at 36 months	