New Guidelines on Stroke Prevention for AF: Europe, Far East or USA, NICE or Not?

The NICE Guidelines

I Savelieva
St George’s University of London, UK
Declaration of Interest


PI: Bayer Pharma AG, Boehringer Ingleheim, Bristol Myers Squibb, Daiichi, Menarini, Pfizer, Sanofi, Servier, Takeda

Consultant/Advisor/Speaker: Astra Zeneca, Bayer Pharma AG, Boehringer Ingleheim, Bristol Myers Squibb, Daiichi-Sankyo, Gilead, Menarini, Mitsubishi Pharma, MSD, Pfizer, Richmond Pharmacology, Sanofi, Takeda
Value of a Clinical Guideline?

Clinical guidelines can:

- Provide **recommendations** for the treatment and care of people by health professionals
- Be used to develop **standards** to assess the clinical practice of individual health professionals
- Be used in the **education and training** of health professionals
- Help **patients** to make informed decisions
- Improve **communication** between patient and health professional
Offer people with atrial fibrillation a **personalised package of care**. Ensure that the package of care is documented and delivered, and that it includes:

- Stroke awareness and measures to prevent stroke
- Rate control
- Assessment of symptoms for rhythm control
- Psychological support if needed
- Up-to-date and comprehensive education and information on:
  - cause, effects and possible complications of atrial fibrillation
  - management of rate and rhythm control
  - anticoagulation
  - practical advice on anticoagulation in line with recommendations
  - support networks
NICE AF Guidelines: Care Flow

Diagnosis of atrial fibrillation (AF)

Personalised package of care and information

Algorithm 1: Stroke Prevention information

Algorithm 2: Rate control strategies

Algorithm 3: Rhythm control strategies

Algorithm 4: Ablation strategies

Monitoring

NICE 2014
Algorithm 1.  Stroke Prevention

Stroke risk
\(\text{CHA}_2\text{DS}_2\text{-VASc}\)

Bleeding risk
\(\text{HAS-BLED}\)

Discuss risks and benefits of anticoagulation

Identify low risk patients i.e. \(\text{CHA}_2\text{DS}_2\text{-VASc} = 0\) (men) or 1 (women)

\(\text{CHA}_2\text{DS}_2\text{-VASc} = 1\) (M)

Consider oral anticoagulation

\(\text{CHA}_2\text{DS}_2\text{-VASc} \geq 2\)

Offer oral anticoagulation

Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences

Vitamin K antagonists (VKA)

Assess anticoagulation control

Non-VKA oral anticoagulant

Poor control

Non- VKA C/I or not tolerated

LAA occlusion

People who choose not to have treatment

No antithrombotic therapy

Annual review for all patients

Low Risk
**CHA\textsubscript{2}DS\textsubscript{2}-VASc: Contribution of Individual Risk Factors in the Danish Cohort**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Event rates, %</th>
<th>HR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF</td>
<td>1.78</td>
<td>2.69 (1.47 - 4.95)</td>
<td>0.001</td>
</tr>
<tr>
<td>HTN</td>
<td>1.49</td>
<td>2.26 (1.75 - 2.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DM</td>
<td>2.02</td>
<td>3.03 (1.89 - 4.86)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VD</td>
<td>1.47</td>
<td>2.22 (1.49 - 3.30)</td>
<td>&lt;0.0001</td>
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<tr>
<td>65-74 yrs</td>
<td>2.09</td>
<td>3.12 (2.57 - 3.78)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Female</td>
<td>0.82</td>
<td>1.24 (0.98 - 1.57)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Proportion free from TE, %

Risk of Stroke in CHA$_2$DS$_2$-VASc Score 1: the Swedish Cohort

- Swedish nationwide health registries
- Retrospective data collection 2005-2010
- N = 140,420

- Quarantine / blanking period after the index AF diagnosis: 4 weeks
- Follow-up: 5 years

Ischemic stroke: 0.6%
Ischemic stroke, unspecified stroke, TIA, PE: 0.9%
Riks-Stroke registry only: 0.3%
Women: 0.1-0.2%
Men 0.5-0.7%

Annual event rates, %

- + TIA
- + Pulmonary embolism
- + Unspecified stroke/SE
- Ischemic stroke only

Prognosis in Patients With CHA$_2$DS$_2$-VASc 1 Treated or Not Treated According to Guidelines

- Community-based cohort study
- N = 2177 with CHA$_2$DS$_2$-VASc 1 (24% of the total population)
- 53% on OAC
- 1° EP: stroke, SE, death
- Follow-up: 2.7 years

Fauchier L, et al. ESC 2015

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Event free

HR = 0.60 (0.40-0.91), p = 0.02

Treated according to ESC Guidelines (n = 680)
Not treated according to ESC Guidelines (n = 343)

Fauchier L, et al. ESC 2015
Sub-optimal TTR and Risk of Stroke

- Meta-analysis of TTR (%) of AF patients treated with warfarin in the community
- TTR >70% is necessary to reduce stroke risk in patients with CHADS$_2$ score ≥2 compared with the non-warfarin treatment group ($p=0.025$)

Calculate the person’s time in therapeutic range (TTR) at each visit
When calculating TTR:

- Use a validated method such as the Rosendaal method for computer-assisted dosing or proportion of tests in range for manual dosing
- Exclude measurements taken during the first 6 weeks of treatment
- Calculate TTR over a period of at least 6 months. [new 26 2014].

Reassess anticoagulation for a person with poor anticoagulation control shown by any of the following:

- 2 INR values higher than 5 or 1 INR value higher than 8 within the past 6 months
- 2 INR values less than 1.5 within the past 6 months
- TTR less than 65%. [new 2014]
"Efficacy" of Aspirin in BAFTA and AVERROES Trials

**BAFTA:** Fatal or disabling stroke, other intracranial haemorrhage or clinically significant arterial embolism

**AVERROES:** Stroke or systemic embolism

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**BAFTA:**
- Event free survival
- Years after randomisation
- Aspirin: 24 (1.8%)
- Warfarin: 48 (3.8%)
- RR = 0.48 (0.28–0.80)
- p = 0.0027
- Stroke:
  - 0.8% vs 1.8%
  - RR = 0.30 (0.13–0.63)
  - p = 0.0004

**AVERROES:**
- Cumulative Hazard
- Months
- Aspirin 81–324 mg/d
- Apixaban 5 mg bd (in 94% of patients)
- HR = 0.45
- 95% CI = 0.32–0.62
- ARR = 2.1%
- P < 0.001 for superiority

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Do not offer aspirin monotherapy solely for stroke prevention to people with AF. [new 2014]

Only consider dual antiplatelet therapy with aspirin and clopidogrel for stroke prevention if anticoagulation is contraindicated or not tolerated and the person has a CHA₂DS₂-VASc score of 2 or above. [new 2014]
The decision about whether to start treatment with A, D or R should be made after an informed discussion between the clinician and the person about the risks and benefits of A, D or R compared with warfarin. For people who are taking warfarin, the potential risks and benefits of switching to A, D or R should be considered in light of their level of international normalised ratio (INR) control.

[This recommendation is from …. for the prevention of stroke and systemic embolism in atrial fibrillation (NICE technology appraisal guidance xxx).] [20xx]

**Apixaban**

\[ \geq 1 \text{ CHADS}_2 \text{ RF} \]

previous stroke, TIA or SE, LVEF < 40%, HF NYHA ≥ class 2, age ≥ 75 years, or age ≥ 65 years with: DM, CAD or ↑BP.

**Dabigatran**

\[ \geq 1 \text{ CHADS}_2 \text{ RF} \]

**Rivaroxaban**

\[ \geq 1 \text{ CHADS}_2 \text{ RF} \]
GARFIELD Registry: Use of Anticoagulation and Drug Choice

n = 17,475 enrolled in 2010-2014

Camm AJ. ESC 2015
<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Year</th>
<th>Risk stratification</th>
<th>OAC indicated</th>
<th>NOAC preferred</th>
<th>Role of ASA</th>
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</thead>
<tbody>
<tr>
<td>ACCP 9th ed.</td>
<td>2012</td>
<td>CHADS&lt;sub&gt;2&lt;/sub&gt;</td>
<td>YES (≥1)</td>
<td>YES</td>
<td>CHADS&lt;sub&gt;2&lt;/sub&gt; = 0 if pt prefers Rx</td>
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<tr>
<td>ESC (update pending)</td>
<td>2012</td>
<td>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;VASc</td>
<td>YES (≥1)</td>
<td>YES</td>
<td>If OAC cannot be used</td>
</tr>
<tr>
<td>APHRS (update pending)</td>
<td>2013</td>
<td>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;VASc</td>
<td>YES (≥2)</td>
<td>YES (CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;VASc 1 but not Riva)</td>
<td>Not recommended, except pts with CAD/stents/TE</td>
</tr>
<tr>
<td>JCS</td>
<td>2014</td>
<td>CHADS&lt;sub&gt;2&lt;/sub&gt;</td>
<td>YES (≥1)</td>
<td>YES (choice depends on CHADS&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>Not recommended</td>
</tr>
<tr>
<td>CCS update</td>
<td>2014</td>
<td>CHADS&lt;sub&gt;2&lt;/sub&gt;</td>
<td>YES (≥1)</td>
<td>YES</td>
<td>CHADS&lt;sub&gt;2&lt;/sub&gt; = 0 + age &lt; 65 + CAD/PAD</td>
</tr>
<tr>
<td>AHA/ACC/HRS</td>
<td>2014</td>
<td>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;VASc</td>
<td>YES (≥2)</td>
<td>YES (in pts unable to take W)</td>
<td>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;VASc = 1 (or nil, or OAC)</td>
</tr>
<tr>
<td>NICE</td>
<td>2014</td>
<td>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;VASc</td>
<td>YES (≥2 or ≥1 in men)</td>
<td>NO</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

Savelieva I, et al. [In press]
2014 NICE AF Guidelines

Anti-coagulation offered

YES

NO

Consider LAAO if anticoagulation is contraindicated or not tolerated and discuss the benefits and risks of LAAO with the person.

Quality of anticoagulation

Poor

Quality of anticoagulation

Good

NOAC offered as per NICE

Only consider dual anti-platelet therapy for stroke prevention if OAC is not possible and CHA$_2$DS$_2$VASc $\geq$ 2
NICE on Anticoagulation

• Simplifies the approach to stroke prevention and promotes anticoagulation in all but lowest-risk patients
• Promotes annual review of stroke and bleeding risk
• Focuses of quality of anticoagulation control
• Removes the issue of aspirin
• Provides equality of access to VKAs and NOACs
• Provides access to LAA occlusion therapies

Algorithm 2. Rate Control Strategies

Pts with HF, AF with reversible cause or acute onset AF

Offer rhythm control irrespective of symptoms if:
- AF with reversible cause
- HF thought to be due to
- New-onset AF

Assess and offer rate control as the first-line strategy to all

Offer β-blocker or a rate limiting CCB as initial monotherapy.
Be aware of symptoms, heart rate, comorbidities and patient preferences
Consider digoxin monotherapy for non-paroxysmal AF only if sedentary
Do not offer amiodarone for rate control

Still symptomatic with monotherapy, consider combination therapy with 2 of: β-blocker, diltiazem, digoxin

If symptoms uncontrolled

Go to algorithm 3: Rhythm Control

Is patient eligible for a rhythm control strategy?

Yes

Go to algorithm 4: Ablation
Algorithm 3: Rhythm Control Strategies

### Persistent AF

**RESTORATION OF SR**

If drug Rx fails to control AF symptoms or is unsuitable:

- Dronedarone (in accordance with STA)

  ? need for drug therapy for long-term rhythm control: associated comorbidities, AAD risks, recurrence of AF

  - For drug therapy for long-term rhythm control offer a \( \beta \)-blocker as 1st line Rx unless there are CIs
  - If \( \beta \)-blocker are contraindicated/unsuccessful, assess the suitability of alternative drugs

- Consider amiodarone for LV impairment or HF

- Do not offer class 1 AADs e.g., flecainide/propafenone in ischaemic or SHD

- Be aware risks of antiarrhythmic sotalol doses, for people with renal failure or low body weight

  **Dronedarone** (in accordance with STA)

**MAINTENANCE OF SR**

- Go to algorithm 4: Ablation Strategy

### Paroxysmal AF

**MAINTENANCE OF SR**

- See later

**PILL IN THE POCKET**

- Symptoms continue

  - LV↓ or HF?

  - SHD?

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AAD: Antiarrhythmic Drug
AADs: Antiarrhythmic Drugs
AADs: Antiarrhythmic Drugs
SHD: Structural Heart Disease
Where people have infrequent paroxysms and few symptoms, or where symptoms are induced by known precipitants (such as alcohol, caffeine), a ‘no drug treatment’ strategy or a ‘pill-in-the-pocket’ strategy should be considered and discussed with the patient.

In people with paroxysmal atrial fibrillation, a 'pill-in-the-pocket' strategy should be considered for those who:

- have no history of left ventricular dysfunction, or valvular or ischaemic heart disease and
- have a history of infrequent symptomatic episodes of paroxysmal atrial fibrillation; and
- have a systolic blood pressure greater than 100 mmHg and a resting heart rate above 70 bpm and
- are able to understand how to, and when to, take the medication.
Algorithm 4: Left Atrial Ablation

Is AF permanent?

- **YES**
  - Consider pace/AVN ablate strategy symptoms or LV dysfunction due to high ventricular rates.

- **NO**
  - Reassess symptoms and the consequent need for ablation after pacing, and drug treatment optimised.

Cardiac surgery planned?

- **NO**
  - Consider LA C ablation before pacing/AVN ablation with paroxysmal AF, or HF due paroxysmal or persistent AF.

- **YES**
  - Offer LA S ablation for symptomatic AF with other CT surgery.

If drugs fail to control symptoms or are unsuitable:

- **Offer** LA C ablation for **paroxysmal AF**.
- **Consider** LA S or C ablation for **persistent AF**.
- **Discuss** the risks and benefits.

AF = atrial fibrillation  
LV = left ventricular  
HF = heart failure  
LA = left atrial  
C = catheter  
S = surgical

NICE 2014
Conclusions

- NICE Guidelines offer a structured, patient-centered approach to management of AF
- NICE Guidelines follow the ESC recommendations on stroke risk stratification and prevention, including LAAO devices
- NICE Guidelines adopt rate control as first-line therapy in patients who are asymptomatic
- NICE Guidelines consider rhythm control an appropriate strategy for symptomatic patients
- NICE Guidelines regard left atrial ablation a valuable therapy, but exercise a more conservative approach to using it as first-line therapy
Thank you!