Update: Prevention after Stroke

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Disclosures

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Amgen; Bayer; BMS/Pfizer; Boehringer-Ingelheim; Elpen; European Union; Galenica; Sanofi; Winmedica
Atrial fibrillation
- Aspirin for AF patients?
- NOAC or VKA?
- SAME-TTR to select oral anticoagulant?
- When to restart OAC after ischemic stroke?
- Is there a role for left atrial appendage occlusion?
- Carotid filter for stroke prevention?

Heart failure with sinus rhythm
- Is there a role for OAC?

Atherosclerotic stroke
- low-dose rivaroxaban & aspirin
- LDL targets

Minor strokes
- Dual antiplatelet treatment: for how long?

PFO
- Closure or medical treatment?
- OAC or aspirin in non-closed PFOs?

ESUS
- ESUS vs. cryptogenic
- NAVIGATE ESUS and RE-SPECT ESUS results
- Potential explanation and implications for future research
Aspirin for AF patients? - ESC Guidelines 2010

CHADS₂ score ≥ 2⁺

- No
- Yes

Consider other risk factors*?
- No
- Yes

Age ≥ 75 years
- No
- Yes

≥ 2 other risk factors*?
- No
- Yes

≥ 2 other risk factors*?
- No
- Yes

I other risk factor*?
- No
- Yes

OAC

OAC (or aspirin)

Nothing (or aspirin)

* Other clinically relevant non-major risk factors: age 65–74, female sex, vascular disease

⁺ Congestive heart failure, Hypertension. Age ≥ 75 years Diabetes. Stroke/TIA/thrombo-embolism (doubled)


A Stroke or Systemic Embolism
Hazard ratio with apixaban, 0.45
(95% CI: 0.32–0.62)

Apixaban

Aspirin

P<0.001

No. at Risk
Aspirin 2791 2716 2530 2112 1543 628
Apixaban 2808 2758 2566 2125 1522 615

B Major Bleeding
Hazard ratio with apixaban, 1.13
(95% CI: 0.74–1.75)

Apixaban

Aspirin

P=0.57

No. at Risk
Aspirin 2791 2738 2557 2140 1571 642
Apixaban 2808 2759 2566 2120 1521 622

Huisman, et al. JACC 2017
Connolly, et al. NEJM 2011
NOAC vs. VKA?

**Study or Subgroup**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Peto Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARISTOTLE</td>
<td>0.40 [0.24, 0.68]</td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48 (60mg)</td>
<td>0.57 [0.36, 0.90]</td>
</tr>
<tr>
<td>RELY (150mg)</td>
<td>0.43 [0.24, 0.79]</td>
</tr>
<tr>
<td>ROCKET-AF</td>
<td>0.73 [0.47, 1.13]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>0.54 [0.42, 0.70]</td>
</tr>
</tbody>
</table>

*Favours non-VKA*  | *Favours warfarin* |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>1.0</td>
</tr>
<tr>
<td>0.1</td>
<td>0.9</td>
</tr>
<tr>
<td>0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>0.7</td>
<td>0.3</td>
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<tr>
<td>0.8</td>
<td>0.2</td>
</tr>
<tr>
<td>0.9</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**Nonvitamin-K-antagonist oral anticoagulants versus warfarin in patients with atrial fibrillation and previous stroke or transient ischemic attack: An updated systematic review and meta-analysis of randomized controlled trials**

George Ntaios1, Yiannis Papavassiliou2, Hans-Chris Diener2, Konstantinos Makartitis1 and Patrik Michel1

Abstract

**Background:** In a previous systematic review and meta-analysis, we assessed the efficacy and safety of nonvitamin-K antagonist oral anticoagulants versus warfarin in patients with atrial fibrillation and stroke or transient ischemic attack. Since then, new information became available.

**Aims:** The aim of the present work was to update the results of the previous systematic review and meta-analysis.

**Methods:** We searched PubMed until 24 August 2016 for randomized controlled trials using the following search terms: "oral rivaroxaban" and "oral dabigatran" and "oral edoxaban" and "oral apixaban" and "previous stroke or transient ischemic attack" and "control group warfarin" and "oral anticoagulants currently on the market or within the intention to be brought to the market in North America or Europe". The outcomes assessed in the efficacy analysis included stroke or systemic embolism, intracranial bleeding, and major or minor hemorrhage. The outcomes assessed in the safety analysis included major bleeding, intracranial bleeding, and major gastrointestinal bleeding. We performed fixed-effects analysis on intention-to-treat basis.

**Results:** Among 183 potentially eligible trials, four were included in the meta-analysis. In total, 25,000 patients, compared to warfarin, nonvitamin-K antagonist oral anticoagulants were associated with a significant reduction in stroke and systemic embolism, intracranial bleeding, major or minor hemorrhage, and major gastrointestinal bleeding. The risk reduction for stroke or systemic embolism, intracranial bleeding, and major or minor hemorrhage, and major gastrointestinal bleeding ranged from 12% to 50%.

**Conclusions:** This updated meta-analysis in 25,000 atrial fibrillation patients with previous stroke or transient ischemic attack shows that compared to warfarin, nonvitamin-K antagonist oral anticoagulants are associated with a significant reduction of stroke, systemic embolism, intracranial bleeding, and gastrointestinal bleeding.
NOAC vs. VKA? – ESC Guidelines 2016

Estimate stroke risk based on number of CHA₂DS₂-VASc risk factors³

- 0⁴:
  - No antiplatelet or anticoagulant treatment (IIIB)

- 1:
  - OAC should be considered (IIaB)

- ≥2:
  - Oral anticoagulation indicated
    - Assess for contra-indications
    - Correct reversible bleeding risk factors

- NOAC (IA)⁵
- VKA (IA)⁶

SAME-TT₂R₂ for OAC selection

<table>
<thead>
<tr>
<th>Condition/influencing factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female)</td>
<td>1</td>
</tr>
<tr>
<td>Age (&lt;60 years)</td>
<td>1</td>
</tr>
<tr>
<td>Medical history (history of more than two of the following: hypertension, diabetes, CAD, PAD, heart failure, stroke; pulmonary, hepatic, or renal disease)</td>
<td>1</td>
</tr>
<tr>
<td>Treatment (interacting medications e.g. amiodarone)</td>
<td>1</td>
</tr>
<tr>
<td>Tobacco use (within 2 years)</td>
<td>2</td>
</tr>
<tr>
<td>Race (non-Caucasian)</td>
<td>2</td>
</tr>
</tbody>
</table>

Patient with AF, newly diagnosed
Needs OAC

Step 3
Decide NOAC or VKA
Calculate SAMe-TT₂R₂ score

If score = 0–2
VKA
Reassess adherence and TTR*
Aim for TTR > 70%

If score > 2
NOAC
Poor TTR**

Lip, et al. Nature Reviews 2018
Start anticoagulants - how soon (or late)?
Ischaemic stroke or TIA

- TIA: After 1 day
- Mild stroke (NIHSS<8): After 3 days
- Moderate stroke (NIHSS 8–16): Exclude haemorrhagic transformation by CT or MRI at day 6, Start after 6 days
- Severe stroke (NIHSS>16): Exclude haemorrhagic transformation by CT or MRI at day 12, Start after 12 days

Left atrial appendage occlusion
Left atrial appendage occlusion vs. OAC

Holmes, et al. JACC 2015

Left Atrial Appendage Closure as an Alternative to Warfarin for Stroke Prevention in Atrial Fibrillation

A Patient-Level Meta-Analysis

David B. Holmes, Jr, MD, Shephal V. Desai, MD, Sahgal Rao, MD, Matthew J. Price, MD, Jose M. Sanchez, MD, Scott O. Schaff, MD, Miguel Valderrabano, MD, Vivit Y. Reddy, MD

BACKGROUND: The risk-benefit ratio of left atrial appendage closure (LAAC) versus systemic therapy (warfarin) for prevention of stroke, systemic embolism, and cardiovascular death in nonvalvular atrial fibrillation (NVAF) requires continued evaluation.

OBJECTIVES: This study sought to assess composite data regarding left atrial appendage closure (LAAC) in 2 randomized trials compared to warfarin for prevention of stroke, systemic embolism, and cardiovascular death in patients with nonvalvular AF.

METHODS: Our meta-analysis included 21,088 patient-years (PY) of follow-up from the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) and PREVAIL (Prospective Randomized Evaluation of the WATCHMAN Left Atrial Appendage Occlusion Device in Patients With Atrial Fibrillation Versus Long-Term Warfarin Therapy) trials and their respective registries (Continued Access to PROTECT AF registry and Continued Access to PREVAIL registry).

RESULTS: With a mean follow-up of 2.69 years, patients receiving LAAC with the WATCHMAN device had significantly fewer hemorrhagic strokes (0.35 vs. 0.56 events/100 patient-years [PY], p < 0.001, adjusted hazard ratio [HR] 0.62, 95% CI 0.42-0.92) and non-CABG-related ischemic strokes (0.19 vs. 0.27 events/100 PY, HR 0.71, 95% CI 0.48-1.09) compared with warfarin. All-cause stroke or systemic embolism was similar between both strategies (1.12% vs. 1.24% PY, HR 0.91, 95% CI 0.62-1.36). There were more ischemic strokes in the device group (3.8 vs. 2.1% PY, HR 1.83, 95% CI 1.23-2.72, respectively), but this trend was not statistically significant. Both trials and registries identified similar event rates and consistent device effect in multiple subgroups.

CONCLUSIONS: In patients with NVAF at increased risk for stroke or bleeding who are candidates for chronic anticoagulation, LAAC resulted in improved rates of hemorrhagic stroke, cardioembolic stroke, and non-CABG-related ischemic stroke compared to warfarin. (J Am Coll Cardiol 2016;68:646-654) © 2016 by the American College of Cardiology Foundation.)
Left atrial appendage occlusion – ESC Guidelines 2016

1. Mechanical heart valves or moderate or severe mitral stenosis
   - Yes
   - No

2. Estimate stroke risk based on number of CHA₂DS₂-VASC risk factors
   - 0
     - No antiplatelet or anticoagulant treatment (IIIB)
   - 1
     - OAC should be considered (IIaB)
   - ≥2
     - Oral anticoagulation indicated
       - Assess for contra-indications
       - Correct reversible bleeding risk factors

3. LAA occluding devices may be considered in patients with clear contra-indications for OAC (IIbC)

4. NOAC (IA)√

5. VKA (IA)cd

Carotid filter for stroke prevention

Reddy, et al. JACC 2019
Atrial fibrillation
- Aspirin for AF patients?
- NOAC or VKA?
- SAME-TTR to select oral anticoagulant?
- When to restart OAC after ischemic stroke?
- Is there a role for left atrial appendage occlusion?
- Carotid filter for stroke prevention?

Heart failure with sinus rhythm
- Is there a role for OAC?
Heart failure with sinus rhythm: a prothrombotic condition

N Engl J Med 1997; 336:251-7
Heart failure with sinus rhythm: is there a role for OAC?

**Green**: stroke reduction  
**Red**: hemorrhage risk

- 0.60 (0.46-0.78)
- 1.92 (1.51-2.45)
Atrial fibrillation
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Atherosclerotic stroke
- low-dose rivaroxaban & aspirin
- LDL targets
### Atherosclerotic strokes: COMPASS

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic or uncertain type</td>
<td>0.51 (0.38–0.68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.70 (1.40–2.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Net-clinical-benefit outcome: CV death, stroke, myocardial infarction, fatal bleeding, or symptomatic bleeding into critical organ</td>
<td>0.80 (0.70–0.91)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Eikelboom, et al. NEJM 2017*
Atherosclerotic strokes: LDL targets

ESC/EAS Guidelines, Eur Heart Journal 2019
Algorithm for LDL management

1. High potency statin at highest recommended / tolerable dose to reach the goal

2. LDL-C goal reached?
   - **Y**: Follow-up Annually, or more frequently if indicated
   - **N**: Add ezetimibe

3. LDL-C goal reached?
   - **Y**: Follow-up Annually, or more frequently if indicated
   - **N**: Add PCSK9 inhibitor

ESC/EAS Guidelines, Eur Heart Journal 2019
Atrial fibrillation
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Minor strokes
- Dual antiplatelet treatment: for how long?
Dual antiplatelet in the early phase of minor stroke

- Major ischemic event
  - Cumulative Probability of Major Ischemic Event (%)
  - Time Since Randomization, d
  - Aspirin
  - Clopidogrel-aspirin

- Major hemorrhage
  - Cumulative Probability of Major Hemorrhage (%)
  - Time Since Randomization, d
  - Aspirin
  - Clopidogrel-aspirin
Disclosures

Pan et al., JAMA Neurology 2019

Dual antiplatelet in the early phase of minor stroke
**Agenda**

**Atrial fibrillation**
- Aspirin for AF patients?
- NOAC or VKA?
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- Is there a role for OAC?

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- LDL targets

**Minor strokes**
- Dual antiplatelet treatment: for how long?

**PFO**
- Closure or medical treatment?
- OAC or aspirin in non-closed PFOs?
PFO closure

- **Green**: stroke reduction all patients
  - $0.43 [0.21, 0.90]

- **Red**: stroke reduction high risk PFOs
  - $0.39 [0.16, 0.96]

- **Orange**: stroke reduction low risk PFOs
  - $0.79 [0.43, 1.43]
OAC vs aspirin for non-closed PFO

**Green**: stroke reduction

**Red**: hemorrhage risk

---

0.68 [0.32–1.48]  
1.61 [0.69-3.73]

---

Favours anticoagulants  
Favours antiplatelets
Atrial fibrillation
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ESUS
- ESUS vs. cryptogenic
- NAVIGATE ESUS and RE-SPECT ESUS results
- Potential explanation and implications for future research
ESUS vs. cryptogenic

- Not investigated
- Multiple causes
- Really cryptogenic

Cryptogenic
ESUS are frequent
ESUS: high recurrence rate

![Graph showing risk of stroke recurrence over time for different stroke subtypes.](Ntaios_Michel_etal_Stroke_2015.png)

**Background and Purpose:** Information about outcomes in Embolic Strokes of Undetermined Source (ESUS) patients is unavailable. This study set forth to investigate outcomes of ESUS patients according to the Athens Stroke Registry and to compare them with patients with other subtypes of stroke.

**Methods:** A retrospective analysis of all ESUS patients treated from 2007 to 2013 was conducted. Patients were categorized based on clinical presentation, and follow-up data were collected. Outcome measures included mortality, recurrence, and secondary prevention.

**Results:** Among the 123 ESUS patients included in the study, 34.5% experienced a recurrent stroke within 5 years. The recurrence rate was highest in the first year (15.8%) and decreased thereafter. The most common subtypes were cardioembolic (30.8%), large-artery atherosclerotic (27.0%), and lacunar (19.7%). No significant differences were found in outcomes between subtypes.

**Conclusions:** ESUS patients have a higher risk of recurrent stroke compared to other subtypes. Early intervention and secondary prevention strategies are crucial to improve outcomes.

**Key Words:** embolic stroke of undetermined source, ESUS, mortality, outcome, stroke recurrence.
ESUS: Potential embolic sources

**Covert Atrial Fibrillation**
- Cancer associated
  - Covert non-bacterial thrombotic endocarditis
  - Tumour emboli from occult cancer

**Arteriogenic emboli**
- Aortic arch atherosclerotic plaques
- Cerebral artery non-stenotic plaques with ulceration

**Paradoxical embolism**
- Patent foramen ovale
- Atrial septal defect
- Pulmonary arteriovenous fistula

**Minor-risk potential cardioembolic sources**

**Mitral or Aortic valve**
- Myxomatous valvulopathy with prolapse
- Mitral annular calcification
- Aortic valve stenosis or Calcific aortic valve

**Non-AF atrial dysrhythmias and stasis**
- Atrial asystole and sick-sinus syndrome
- Atrial high-rate episodes
- Atrial appendage stasis with reduced flow velocities or spontaneous echodensities

**Atrial structural abnormalities**
- Atrial septal aneurysm or Chiari network

**Left ventricle**
- Moderate systolic or diastolic dysfunction (global or regional)
- Ventricular non-compaction or Endomyocardial fibrosis

**ESUS**: 90% are treated with antiplatelets

<table>
<thead>
<tr>
<th>Study</th>
<th>Antithrombotic Therapy</th>
<th>AF During Follow-Up†</th>
<th>Stroke (Est Annualized Rate)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ntaios et al(^{13,26})‡</td>
<td>74% APT only, 22% OAC</td>
<td>80 (29%)</td>
<td>6.8%/y</td>
</tr>
<tr>
<td>Li et al(^{15})</td>
<td>NR</td>
<td>NR</td>
<td>≈5%/y</td>
</tr>
<tr>
<td>Putaala et al(^{16})‡</td>
<td>85% APT, 11% OAC</td>
<td>NR</td>
<td>5.1%/y</td>
</tr>
<tr>
<td>Ntaios et al(^{24})‡</td>
<td>87% APT only, 12% OAC</td>
<td>NR</td>
<td>4.8%/y</td>
</tr>
<tr>
<td>Masina et al(^{12})¶</td>
<td>99% APT</td>
<td>NR</td>
<td>2.3%/y</td>
</tr>
<tr>
<td>Ueno et al(^{22})#</td>
<td>72% APT, 29% OAC</td>
<td>NR</td>
<td>3.9%/y</td>
</tr>
<tr>
<td>Arauz et al(^{23})¶</td>
<td>91% APT, 5% OAC</td>
<td>NR</td>
<td>2.3%/y</td>
</tr>
<tr>
<td>Pooled – unweighted average‡, ††</td>
<td>87% APT, 12% OAC</td>
<td>...</td>
<td>4.0%/y</td>
</tr>
<tr>
<td>Pooled – weighted average‡, ††</td>
<td>86% APT, 13% OAC</td>
<td>...</td>
<td>4.5%/y</td>
</tr>
</tbody>
</table>
New AF after stroke without cause (CRYSTAL – AF)

Hazard ratio, 8.8 (95% CI, 3.5–22.2)
P<0.001 by log-rank test
Stroke reduction

Hemorrhage risk

Hart, et al. NEJM 2018
**RE-SPECT ESUS**

**Stroke reduction**

HR 0.84; 95% CI: 0.68-1.03

**Hemorrhage risk**

HR 1.19; 95% CI: 0.85-1.66
AVERROES

### Stroke or Systemic Embolism

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
<th>Aspirin</th>
<th>Apixaban</th>
<th>Hazard Ratio with Apixaban (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior stroke or TIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No</td>
<td>4835</td>
<td>80 (3.0)</td>
<td>41 (1.5)</td>
<td></td>
<td>0.18</td>
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<tr>
<td>Yes</td>
<td>764</td>
<td>36 (8.3)</td>
<td>10 (2.5)</td>
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### Abstract

**Background:** Vitamin K antagonists have been shown to prevent stroke in patients with atrial fibrillation. However, many patients are not suitable candidates for or are unwilling to receive vitamin K antagonists due to the inherent risk of stroke. Apixaban, a novel factor Xa inhibitor, may be an alternative treatment for such patients.

**Methods:** In a double-blind study, we randomly assigned 1878 patients with atrial fibrillation who were at increased risk for stroke and believed to be unsuitable for warfarin to receive apixaban (at a dose of 5 mg twice daily) or aspirin (100 to 325 mg per day). The primary outcome was the occurrence of stroke or systemic embolism.

**Results:** Before enrollment, 40% of the patients had received vitamin K antagonists. The primary outcome occurred in 5.6% of patients assigned to apixaban and 7.3% of those assigned to aspirin (hazard ratio, 1.13; 95% confidence interval, 0.82 to 1.56; P = .42). The rate of death due to stroke or systemic embolism was 1.4% in the apixaban group and 2.1% in the aspirin group (hazard ratio, 0.67; 95% CI, 0.32 to 1.37; P = .24). There were 11 cases of intracranial hemorrhage in the aspirin group and 13 cases in the apixaban group (hazard ratio, 1.17; 95% CI, 0.67 to 2.00; P = .65). The treatment effects were consistent among important subgroups. A post-hoc analysis of the AVERROES trial showed that apixaban was associated with a lower risk of stroke compared to aspirin (hazard ratio, 0.59; 95% CI, 0.37 to 0.93; P = .02).

**Conclusions:** In patients with atrial fibrillation for whom vitamin K antagonists are unsuitable, apixaban reduced the risk of stroke or systemic embolism without significantly increasing the risk of major bleeding or intracranial hemorrhage.

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**References:**

ESUS: red & white thrombi
ESUS: Overlap of potential embolic sources

1 = Atrial cardiopathy
2 = Arterial disease
3 = Left ventricular disease
4 = Cardiac valvular disease
5 = PFO
6 = Cancer

Ntaios, Michel, et al. JAHA 2019
ESUS: Implications for future research

ESUS

+ NOAC

Red-thrombi
PES

White-thrombi
PES

+ Aspirin

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Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease


ABSTRACT

We evaluated whether rivaroxaban alone or in combination with aspirin would be more effective than aspirin alone for secondary cardiovascular prevention.

METHODS

In this double-blind trial, we randomly assigned 27,396 participants with stable atherosclerotic vascular disease to receive rivaroxaban (2.5 mg twice daily), plus aspirin (100 mg once daily), or rivaroxaban (5 mg twice daily), or aspirin (300 mg once daily). The primary outcome was a composite of cardiovascular death, stroke, or myocardial infarction. The study was stopped for superiority of the rivaroxaban-plus-aspirin group after a mean follow-up of 23 months.

RESULTS

The primary outcome occurred in fewer patients in the rivaroxaban-plus-aspirin group than in the aspirin-alone group (17 patients [4.4%] vs. 46 patients [5.4%], hazard ratio: 0.76; 95% confidence interval: 0.66 to 0.86; P = 0.001; z = 2.4126). Major bleeding events occurred in more patients in the rivaroxaban-plus-aspirin group (1.9% vs. 0.4%, 1.6% vs. 0.1%, 1.5% vs. 0.1%; P = 0.01). There was no significant difference in intracranial or fatal stroke-aspirin group as compared with the rivaroxaban group (hazard ratio: 0.32; 95% CI: 0.27 to 0.37; P = 0.001). The primary outcome did not occur in significantly fewer patients in the rivaroxaban-plus-aspirin group than in the aspirin-alone group, but major bleeding events occurred in more patients in the rivaroxaban-alone group.

CONCLUSIONS

Among patients with stable atherosclerotic vascular disease, those assigned to rivaroxaban (2.5 mg twice daily) plus aspirin had better cardiovascular outcomes and more major bleeding events than those assigned to aspirin alone, while the rivaroxaban group had reduced bleeding events (relative risk: 0.32; 95% CI: 0.27 to 0.37; P = 0.001). The primary outcome did not occur in significantly fewer patients in the rivaroxaban-plus-aspirin group than in the aspirin-alone group, but major bleeding events occurred in more patients in the rivaroxaban-alone group.
Take-home messages

Atrial fibrillation
- Aspirin for AF patients? → NO
- NOAC or VKA? → NOACs
- SAME-TTR to select oral anticoagulant? → Maybe, but not sure if improves outcomes
- When to restart OAC after ischemic stroke? → 1-3-6-12
- Is there a role for left atrial appendage occlusion? → If OAC is contraindicated, perhaps
- Carotid filter for stroke prevention? → Too premature

Heart failure with sinus rhythm
- Is there a role for OAC? → No

Atherosclerotic stroke
- low-dose rivaroxaban & aspirin → Significant net clinical benefit
- LDL targets → <55mg/dl (1.42mmol/l)

Minor strokes
- Dual antiplatelet treatment: for how long? → ~3 weeks

PFO
- Closure or medical treatment? → Closure for <60 years, especially if higher risk PFOs
- OAC or aspirin in non-closed PFOs? → Aspirin

ESUS
- ESUS vs. cryptogenic → ESUS
- NAVIGATE ESUS and RE-SPECT ESUS results → Negative
- Potential explanation and implications for future research → overlap of red & white thrombi