Initiating anticoagulation in Atrial Fibrillation

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UCL Partners
Current management of stroke prevention in AF in clinical practice in England

Patients for whom anticoagulant therapy is indicated (CHADS₂ score ≥1)

- Anticoagulant: 45%
- Anticoagulant + aspirin: 26%
- Not receiving treatment: 11%
- Aspirin: 11%
- Others*: 7%

* 'Others' denote patients treated with just aspirin and other antiplatelet agents that cannot tolerate anticoagulants or refuse to take them

<table>
<thead>
<tr>
<th>July-Sept 2013 Total strokes</th>
<th>17,540</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known AF prior to admission</td>
<td>3461 (19.8%)</td>
</tr>
<tr>
<td>On oral antiplatelets</td>
<td>1,489 (43%)</td>
</tr>
<tr>
<td>On oral anticoagulation</td>
<td>1,329 (38.4%)</td>
</tr>
<tr>
<td>Contra-indicated to anticoagulation</td>
<td>408 (11.8%)</td>
</tr>
</tbody>
</table>
Older AF patients less likely to get warfarin
The paths from research to improved health outcomes

• Awareness
• Acceptance
• Applicable
• Available and Able
• Acted on
• Agreed to
• Adhered to
The paths from research to improved health outcomes

- Awareness
- Acceptance
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- Agreed to
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P Glasziou, B Haynes. EBM 2005; 10: 4-7

Clinical Quality Improvement
Initiating oral anticoagulation in AF

- Patient assessment
- Risk mitigation
- Anticoagulant selection
Initiating oral anticoagulation in AF
- Patient assessment

- Congestive heart failure/ LV dysfunction 1
- Hypertension 1
- Age ≥ 75 2
- Diabetes mellitus 1
- Stroke/TIA/TE 2
- Vascular disease 1
  (CAD, CArD, PAD)
- Age 65-74 1
- Sex category (female) 1

<table>
<thead>
<tr>
<th>Score</th>
<th>Annual stroke rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>3</td>
<td>3.2</td>
</tr>
<tr>
<td>4</td>
<td>4.0</td>
</tr>
<tr>
<td>5</td>
<td>6.7</td>
</tr>
<tr>
<td>6</td>
<td>9.8</td>
</tr>
<tr>
<td>7</td>
<td>9.6</td>
</tr>
<tr>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>9</td>
<td>15.2</td>
</tr>
</tbody>
</table>

Consider anticoagulation for men CHADSVASc -1
Offer anticoagulation CHADSVASc -2 or more
Initiating oral anticoagulation in AF - risk mitigation

• HASBLED – correctable risk factors (Not to exclude)
  – Hypertension (systolic blood pressure > 160mmHg
  – Labile INR’s
  – Drugs (antiplatelet agents, NSAIDs, or alcohol excess
  – Abnormal liver disease? Are the LFT's abnormal?
  – active bleeding lesions/ bleeding tendencies/ coagulation defects

• Other considerations
  – poor literacy or difficulty understanding management?
  – History of non compliance

• Refer people with a history of intracranial haemaorrhage
Importance of Influence

Proportion of those with AF
NOT on warfarin/parent. anticoag
no major contraindications
Warfarin is underused - Why?

**Patient factors**
- Refusal, perceived inconvenience
- Responsibility associated with INR monitoring
- Inadequate knowledge

**Physician factors**
- Over-estimation of potential bleeding and falls risk
- Safety factors/monitoring
Prescribing for AF 2008-13 Newham APEL

- Guideline
- Education
- Audit
- IT tools
- No money

On anticoagulant:
- 2 year improvement
- 10% increase in anticoagulation
- 10% decrease in antiplatelets

On antiplatelet:

On neither:

Percentage of AF patients

Apr-08 Apr-09 Apr-10 Apr-11 Apr-12 Apr-13
### Medicines Optimisation - CCG Dashboard

**Newer Oral Anticoagulants (NOAC)**

<table>
<thead>
<tr>
<th>CCG Code</th>
<th>CCG Name</th>
<th>Dabigatran etexilate &amp;</th>
<th>Dabigatran etexilate,</th>
<th>Indicator [ITEMS/ITEMS]</th>
</tr>
</thead>
<tbody>
<tr>
<td>08V</td>
<td>NHS Tower Hamlets CCG</td>
<td>142</td>
<td>4,660</td>
<td>3.0</td>
</tr>
<tr>
<td>07T</td>
<td>NHS City and Hackney CCG</td>
<td>232</td>
<td>5,611</td>
<td>4.1</td>
</tr>
<tr>
<td>08M</td>
<td>NHS Newham CCG</td>
<td>113</td>
<td>7,161</td>
<td>1.6</td>
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<tr>
<td>08W</td>
<td>NHS Waltham Forest CCG</td>
<td>186</td>
<td>5,880</td>
<td>3.2</td>
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<tr>
<td>07L</td>
<td>NHS Barking and Dagenham CCG</td>
<td>204</td>
<td>7,852</td>
<td>2.6</td>
</tr>
<tr>
<td>08N</td>
<td>NHS Redbridge CCG</td>
<td>258</td>
<td>7,255</td>
<td>3.6</td>
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<tr>
<td>08F</td>
<td>NHS Havering CCG</td>
<td>349</td>
<td>7,078</td>
<td>4.9</td>
</tr>
</tbody>
</table>

The number of prescription items for apixaban, dabigatran etexilate and rivaroxaban as a percentage of the total number of prescription items for apixaban, dabigatran etexilate, rivaroxaban and warfarin sodium.
# Stroke Prevention: Anticoagulant Effect

## Meta-analysis of stroke or systemic embolism

<table>
<thead>
<tr>
<th>Category</th>
<th>Relative Hazard Ratio (95% CI)</th>
<th>Favours warfarin</th>
<th>Favours other Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>W vs Placebo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs W_{low dose}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Aspirin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Aspirin + Clop</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Ximelagatran</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Dabigatran 110</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Rivaroxaban</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Dabigatran 150</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Apixaban 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Dabigatran 110</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Rivaroxaban</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Dabigatran 150</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W vs Apixaban 5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Modified from Camm AJ. EHJ 2009;30:2554-5*
On the 20th of May 1747, I selected twelve patients in the scurvy, on board the Salisbury at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots and lassitude, with weakness of their knees. They lay together in one place, being a proper apartment for the sick in the forehold; and had one diet common to all, viz. water-gruel sweetened with sugar in the morning; fresh mutton-broth often times for dinner; at other times light puddings, boiled biscuit with sugar, &c. and for supper, barley and raisins, rice and currants, sago and wine, or the like. Two of these were ordered each a quart of cyder a day. Two others took twenty-five drops of elixir vitriol.

1747
Lind’s Trial

1753
Findings Published

1794
Lemon juice issued on non-stop voyage to India

1795
Routine adoption: lemon juice to whole fleet

Delayed adoption: wasted opportunities; lost lives
How fast do useful new treatments get to patients?

Research into routine practice = 17 years
Average annual rate of adoption = 3.2 %

<table>
<thead>
<tr>
<th>Clinical Procedure</th>
<th>Landmark Trial</th>
<th>Rate of Use study</th>
<th>Rate of Use %</th>
<th>Annual increase in Rate of Use %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu Vaccination</td>
<td>1968</td>
<td>1997</td>
<td>55</td>
<td>1.9</td>
</tr>
<tr>
<td>Thrombolytic therapy</td>
<td>1971</td>
<td>1989</td>
<td>20</td>
<td>1.1</td>
</tr>
<tr>
<td>Pneumococcal vaccination</td>
<td>1977</td>
<td>1997</td>
<td>35.6</td>
<td>1.8</td>
</tr>
<tr>
<td>Diabetic eye exam</td>
<td>1981</td>
<td>1997</td>
<td>38.4</td>
<td>2.4</td>
</tr>
<tr>
<td>Beta Blockers after MI</td>
<td>1982</td>
<td>1997</td>
<td>61.9</td>
<td>4.1</td>
</tr>
<tr>
<td>Mammography</td>
<td>1982</td>
<td>1997</td>
<td>70.4</td>
<td>4.7</td>
</tr>
<tr>
<td>Diabetic footcare</td>
<td>1983</td>
<td>1998</td>
<td>20</td>
<td>4.0</td>
</tr>
<tr>
<td>Cholesterol screening</td>
<td>1984</td>
<td>1995</td>
<td>65</td>
<td>5.9</td>
</tr>
<tr>
<td>Fecal occult blood test</td>
<td>1986</td>
<td>1993</td>
<td>17</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Anticoagulation in atrial fibrillation

Anticoagulation

Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist.

1.5.2 Consider anticoagulation for men with a CHA$_2$DS$_2$-VASc score of 1. Take the bleeding risk into account. [new 2014]

1.5.3 Offer anticoagulation to people with a CHA$_2$DS$_2$-VASc score of 2 or above, taking bleeding risk into account. [new 2014]

1.5.4 Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences. [new 2014]

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Do benefits of anticoagulation outweigh risks of bleed?

- Warfarin is drug of first choice unless contraindicated.
- Anticoagulation suitable but warfarin not tolerated/contraindicated.
- Consider NOAC

NOACs should be considered as an alternative to warfarin if...

- warfarin allergy/contraindications
- unable to adhere to monitoring
- unable to achieve INR in range despite adherence to treatment
Apixaban, dabigatran or rivaroxaban

dose based on age & GFR (using Cockcroft Gault for GFR)

- **GFR >50 ml/min**
  - Use Cockcroft Gault to calculate GFR if age >80 years or GFR <60 ml/min
  - Dabigatran 150mg BD
  - Apixaban 5mg BD
  - Rivaroxaban 20mg OD
  - Dabigatran not advised previous MI
  - Reduce dose if additional bleeding risk

- **Age > 80 years or**
  - Dabigatran GFR 30-50 ml/min
  - Apixaban or rivaroxaban GFR 15-50
  - Dabigatran 110mg BD
  - Apixaban 2.5mg BD
  - Rivaroxaban 15mg OD

- **Dabigatran GFR<30 ml/min**
  - Apixaban/rivaroxaban GFR <15 ml/min
  - NOT suitable

Anticoagulation not suitable: only use aspirin or clopidogrel if previous CVD
The paths from research to improved health outcomes

- Awareness
- Acceptance
- Applicable
- Available and Able
- Acted on
- Agreed to
- Adhered to

Decision aids, patient education, compliance aids
Suggested structured follow-up

Initiator of anticoagulant treatment:
- Sets indication for anticoagulation;
- Makes choice of anticoagulant;
- Decides on need of proton pump inhibitor;
- Baseline hemoglobin, renal and liver function;
- Provides education;
- Hands out anticoagulation card;
- Organises follow-up (when, by whom, what?);
- Remains responsible coordinator for follow-up.

First FU: 1 month

Follow-up: GP; anticoagulant clinic; initiator of therapy; ...

Checks:
1. Compliance (patient should bring remaining pills);
2. Thrombo-embolic events;
3. Bleeding events;
4. Other side effects;
5. Co-medications and over-the-counter drugs.
6. Need for blood sampling?

1 m?
3 m
6 m?

In case of problems: contacts initiator of treatment.

Else: fills out anticoagulation card and sets date/place for next follow-up.

www.escardio.org/EHRA
# Checklist during follow-up of AF patients on NOACs

<table>
<thead>
<tr>
<th></th>
<th>Interval</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Compliance             | Each visit     | Inspect remaining medication  
Stress importance of compliance  
Inform about compliance aids     |
| Thrombo-embolism       | Each visit     | Cerebral, systemic and pulmonary circulation                            |
| Bleeding               | Each visit     | “Nuisance” bleeding – prevention possible?  
Bleeding with risk or impact on QoL – prevention possible? Need to revise dose? |
| Side effects           | Each visit     | Continuation? Temporary cessation with bridging? Change of anticoagulant drug? |
| Co-medications         | Each visit     | Prescription or over-the counter drugs?  
Even temporary use can be risky |
| Blood sampling         | Yearly  
6-monthly  
3-monthly on indication | Haemoglobin, renal, liver function  
Renal function if CrCl 30-60 ml/min or if on dabigatran and aged >75 years or fragile  
If CrCl 15-30 ml/min  
If intercurring condition may impact renal or hepatic function. |

www.escardio.org/EHRA
Adherence to new medication

Table 2  Adherence to new medication

<table>
<thead>
<tr>
<th>Nature of problem</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side effects</td>
<td>Numbness, oral thrush, nausea, vomiting, giddiness</td>
</tr>
<tr>
<td></td>
<td>Stopped taking new medicine because of side effects</td>
</tr>
<tr>
<td>Concerns</td>
<td>Not keen – don’t believe in taking pills</td>
</tr>
<tr>
<td></td>
<td>Worried about taking new medicine, for example because of previous side</td>
</tr>
<tr>
<td></td>
<td>effects, allergy, potential interactions</td>
</tr>
<tr>
<td>Practical aspects</td>
<td>Tablets difficult to swallow</td>
</tr>
<tr>
<td></td>
<td>Hard to remember complicated regime</td>
</tr>
<tr>
<td></td>
<td>Have to take half a tablet and hard to break accurately</td>
</tr>
</tbody>
</table>


Effective treatments

BEHAVIOUR

Practitioner – prescribing

Patient - adherence

Optimum outcomes
# Pharmacology of new agents

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran&lt;sup&gt;1-3&lt;/sup&gt;</th>
<th>Rivaroxaban&lt;sup&gt;4,5&lt;/sup&gt;</th>
<th>Apixaban&lt;sup&gt;6,7&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mode of action</strong></td>
<td>Factor II</td>
<td>Factor X</td>
<td>Factor X</td>
</tr>
<tr>
<td><strong>Half life</strong></td>
<td>12-14 hrs</td>
<td>7-11 hrs</td>
<td>12 hrs</td>
</tr>
<tr>
<td><strong>Dosing</strong> (in atrial fibrillation)</td>
<td>B.D.</td>
<td>O.D.</td>
<td>B.D.</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td>Esterase catalysed hydrolysis</td>
<td>CYP P450 dependant and independent mechanisms</td>
<td>CYP P450</td>
</tr>
<tr>
<td><strong>Excretion</strong></td>
<td>85% Renal</td>
<td>1/3 Renal 2/3 Hepatic</td>
<td>1/4 Renal 3/4 Non Renal</td>
</tr>
<tr>
<td><strong>Form</strong></td>
<td>Capsule</td>
<td>Tablet</td>
<td>Tablet</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>150 mg</td>
<td>20 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td></td>
<td>110 mg (&gt;80 yrs, verapamil or increased bleeding risk)</td>
<td>15 mg (CrCL 30-49 ml/min)</td>
<td>2.5 mg (2 or more: &gt;80yr; weight &lt;60 kg; Cr &gt;1.5 mg/dL)</td>
</tr>
</tbody>
</table>


Further information and licensed indications can be found at [http://www.medicines.org.uk/emc/](http://www.medicines.org.uk/emc/)
Adherence programme – Darzi fellow

Referral
from 1°/2° care

Unmet need
Capacity of anticoagulation clinics

Levers
NMS/MURs
Loyalty of patients

Educational Needs
Atrial fibrillation
Anticoagulation
CBT

Patient need
Community pharmacy
New medicines

Referral Process direct to community pharmacy after NOAC Initiation

Evaluation of pathway redesign for patients & professionals
“Drugs don’t work in patients who don’t take them”

C. Everett Koop, MD
**GP Initiation Meeting**

UCLPartners

Monday, 10 November 2014 from 14:30 to 16:30 (GMT)

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**Ticket Information**

<table>
<thead>
<tr>
<th>TYPE</th>
<th>REMAINING</th>
<th>END</th>
<th>QUANTITY</th>
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<tr>
<td>General</td>
<td>32 Tickets</td>
<td>10 Nov 2014</td>
<td>Free</td>
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[Register](https://www.eventbrite.co.uk/e/gp-initiation-meeting-tickets-13582338139)
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