Atrial Fibrillation Symposium
26 June 2015

Welcome
Innovation and Health Connected

Dr Liz Mear
Chief Executive
The North West Coast AHSN

- 15 Academic Health Science Networks across England
- Licensed and funded by NHS England
- Promoting, evidence-based innovation in health and social care
- Single structure to share and disseminate good practice and learning
- Working in partnership and collaboration

Our vision

- Reducing Health Inequalities
- Improving Economic Growth and promoting a vibrant economy
The AHSN Vision

- co-production
- Evidence-based
- culture
- peer support
- patient experience
- excellence
- behaviours
- spread
- implementation
- adoption
- scouts
- Innovation
- Discovery
- journey
- scale & pace
Key Partnerships

SCNs

Cheshire and Merseyside SCN
- Kidney Disease
- Diabetes
- Neurological conditions
- Avoiding frail elderly hospital admission
- Good practice in care homes

GMLSC SCN
- Maternity
- End of Life Care
- Children’s Health
- Kidney Disease
- Learning Disabilities
- Diabetes
- Neurological conditions

Stroke / CVD
- Mental Health
- Dementia
- Cancer

NWC AHSN
- Alcohol abuse
- Musculoskeletal health
- Safety in sepsis / hydration / transitional care
Shaping the future together
2015/16 – In Summary
Work with commissioners and public health

Build a culture of partnership and collaboration

Rapid Spread of Research and Innovation into Practice

Improving Economic Growth

Core Platforms

Safety

Cross Cutting Workstreams

Prevention & early detection of disease

System integration

Reducing health inequalities

Use of technology

Procurement

Innovation culture

Effective partnerships

Digital health / data integration

Resident involvement

Business support

Future workforce

Using Greenspace in health

Precision Medicine

Clinical

Leadership

Paediatric/Adult care transition

Hydration

Sepsis

Technology for safety

Support to avoid frail elderly admissions

Good practice Care Homes programme

Health and wellbeing of staff

Measurement

Medicine optimisation across the system

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Stroke

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Musculoskeletal innovation

Reduce alcohol related A&E attendances

System integration

Use of technology

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Business support

Future workforce

Using Greenspace in health

Precision Medicine
## SCN Business Plan

<table>
<thead>
<tr>
<th>Domain</th>
<th>Area of work</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventing people from dying prematurely</td>
<td>Cardiovascular (Cardiac, stroke, renal, diabetes)</td>
</tr>
<tr>
<td>Enhancing quality of life for people with long term conditions</td>
<td>Mental Health, Dementia and Neurological Conditions, Learning Disabilities</td>
</tr>
<tr>
<td>Helping people to recover from episodes of ill health or following injury</td>
<td>Child and Adolescent Mental Health Services</td>
</tr>
<tr>
<td></td>
<td>Maternity, Children &amp; Young People</td>
</tr>
<tr>
<td></td>
<td>Cancer</td>
</tr>
<tr>
<td>Ensuring that people have a positive experience of care</td>
<td>Patient and Public Involvement</td>
</tr>
<tr>
<td></td>
<td>Tackling Health Inequalities</td>
</tr>
<tr>
<td>Treating and caring for people in a safe environment &amp; protecting them from avoidable harm</td>
<td>Advancing Equality</td>
</tr>
<tr>
<td></td>
<td>Palliative and End of Life Care</td>
</tr>
</tbody>
</table>
Our aims for today

• To support the development of knowledge and understanding in the area of AF.
• To disseminate the AF Lancashire pulse testing campaign,
• To showcase best practice in key theme areas - identify, manage and treat, to encourage attendees to consider the whole pathway.
• To look at innovative projects that are developing to support improvements in AF management.
• To introduce the CCG tool-kit
• To debate issues relating to Atrial Fibrillation
• To allow companies to showcase innovations and supportive tools
The Lancashire ‘Know Your Pulse’ campaign

Atrial Fibrillation
Reducing the number of strokes
in the North West Coast

Dr Julia Reynolds
Programme Manager, North West Coast AHSN
The Problem of Stroke and AF

- 1 in 5 strokes are due to AF (approx 3,000 per year) in the north west
- AF is steadily rising (WHO)
- Strokes due to AF are more serious and debilitating
- Cost implications both to families and carers
- Cost implications for the NHS and the wider economy
Costs of Atrial Fibrillation related stroke in our area.

If medicines were optimised in our area we could save a massive £4,272,000 per year in NWC.

Currently over half of people with AF are either unidentified or not receiving treatment.

Every stroke prevented could save £23,315 2. In England during 2012/13 £103m was spent on AF Ischaemic Strokes which was 37.2% of all ischaemic stroke inpatient costs.
Our Approach to the Programme

- **Innovation**
- *using tools and technologies* to help practitioners to diagnose and manage AF

- **Awareness Raising** – helping the public to become more aware of and understand Atrial Fibrillation

- **Identification** – helping health care practitioners become more confident in managing AF

- **Management** – supporting self management/NICE approved technologies
Raise Awareness

- Identify
- Innovate
- Manage

Working with a range of environments
- Pharmacy
- GP Practices
- Care Homes

Campaigns – Liverpool 2014 Lancashire 2015

- Models of care for anticoagulation
- Online Education for health care practitioners

- Use of technology
- Alive Cor
- MyDiagnostick
- Genotype guided testing
- Self Management
- Technology
- reviews
Our Campaign Partners

Greater Manchester,
Lancashire and South
Cumbria Strategic Clinical
Networks

Lancashire Teaching Hospitals NHS

NHS Foundation Trust

AF Association

British Heart Foundation

Heartbeat

AliveCor

Age UK

Technomed

Healthwatch Lancashire
# The Lancashire AF Campaign (May 2015)

<table>
<thead>
<tr>
<th>Activities</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification, education and awareness raising</td>
<td>workshops (2), meetings/events (4) and drop-ins (4)</td>
</tr>
<tr>
<td>Promotion &amp; Comms</td>
<td>radio, local press, network mailing lists</td>
</tr>
<tr>
<td>Tested over 504 people</td>
<td></td>
</tr>
<tr>
<td>Identified 34 abnormal pulses</td>
<td>advised to visit GP</td>
</tr>
<tr>
<td>Use of technology to support the campaign</td>
<td></td>
</tr>
<tr>
<td>Low cost</td>
<td></td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th>AGE</th>
<th>Number Males</th>
<th>Cases AF</th>
<th>Prevalence</th>
<th>Number Females</th>
<th>Cases AF</th>
<th>Prevalence</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-39</td>
<td>21</td>
<td>1</td>
<td>4.76%</td>
<td>49</td>
<td>2</td>
<td>4.08%</td>
<td>4.42%</td>
</tr>
<tr>
<td>40-49</td>
<td>18</td>
<td>0</td>
<td>0.00%</td>
<td>32</td>
<td>1</td>
<td>3.13%</td>
<td>1.56%</td>
</tr>
<tr>
<td>50-59</td>
<td>29</td>
<td>1</td>
<td>3.45%</td>
<td>58</td>
<td>3</td>
<td>5.17%</td>
<td>4.31%</td>
</tr>
<tr>
<td>60-69</td>
<td>51</td>
<td>5</td>
<td>9.80%</td>
<td>46</td>
<td>1</td>
<td>2.17%</td>
<td>5.99%</td>
</tr>
<tr>
<td>70-79</td>
<td>60</td>
<td>9</td>
<td>15.00%</td>
<td>52</td>
<td>5</td>
<td>9.62%</td>
<td>12.31%</td>
</tr>
<tr>
<td>80+</td>
<td>20</td>
<td>3</td>
<td>15.00%</td>
<td>28</td>
<td>2</td>
<td>7.14%</td>
<td>11.07%</td>
</tr>
<tr>
<td>Total</td>
<td>199</td>
<td>19</td>
<td></td>
<td>265</td>
<td>14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results

Comparison of MyDiagnostick vs Wider Population

- MyDiagnostick
- National Average
Outcome focussed

More people identified (increase prevalence)
More people treated (anti-coagulation)

Less people having strokes (we want to support a 5% reduction over the next 5 years)
Reduced costs of stroke (we estimate that our campaigns have potentially saved £0.5 million per year in earlier identification)

Improved patient and clinician experience through better knowledge and management.
Innovate

Frontline staff have the answers

Work with us to innovate – we can help by being a catalyst

Partnerships between NHS, industry, charity, service users & University
Increasing the prescribing of anticoagulants in general practice: involving pharmacists

Louise Winstanley
Clinical Practice Pharmacist Team Leader
Fylde & Wyre
INCREASING THE PRESCRIBING OF ANTICOAGULANTS IN GENERAL PRACTICE:

IN VOLVING PHARMACISTS

Louise Winstanley
Clinical Practice Pharmacist Team Lead
louisewinstanley@nhs.net
07827 305272
Objectives

• To describe a stepwise approach to:
  • Validating AF registers
  • Increasing numbers of people on registers leading to
  • Increased prevalence

• To define how patients were identified

• To describe different practical approaches to improve:
  • Calculating CHA2DS2 VASc and HAS BLED scores
  • Uptake of OACs
Work in 2013/14
Fylde and Wyre practices

• Rationale for work:
  • NICE guidance due in 2014
  • Strong evidence base for OACs v aspirin
  • Apply CHA2DS2 VASc scores
  • And Has bled scores
  • GRASP tool showed 66 expected strokes a year

• Aims:
  • Patient cohort identified
  • Appropriate anticoagulation management of AF
Work in 2013/14

- Baseline assessment of local AF registers
  - GRASP AF tool: anticoagulant, aspirin, or nil
  - Search of patient records in each GP practice to review diagnosis and management
  - Note that this is time consuming and complex

- Patients on aspirin or nil invited to attend a specialist clinic held in a local GP surgery

- 10 AF clinics on Saturdays
  - attended by 239 patients
Work in 2013/14

At the clinics:

• 1. Group education session about AF and stroke risk, led by a specialist nurse

• 2. Blood pressure and pulse tests with all patients
   • risk of stroke CHA2DS2 VASc and bleeding “HAS BLED” scores

• 3. Individual consultation with cardiology consultant

• Each patient spent approximately 45 minutes in the clinic in total.
PROMs

- Most patients had not previously understood the link between AF diagnosis and stroke risk

- A patient satisfaction survey showed:
  - 99% found the clinic useful
  - 85% said they would attend a similar clinic in the future
  - 93% of patients would recommend the clinic to others
## Outcomes 2013/14

<table>
<thead>
<tr>
<th>QOF AF 1 [Patients on AF Register] (17 practices)</th>
<th>AF Prevalence [Total]</th>
<th>Baseline April 2013</th>
<th></th>
<th>AF Prevalence [Total]</th>
<th>Increase in no of patients on registers</th>
<th>% Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3106</td>
<td>2.3%</td>
<td>3341</td>
<td>2.45%</td>
<td>235</td>
</tr>
</tbody>
</table>

QOF AF 1 [Patients on AF Register] (17 practices)
Prescribing outcomes

Anticoagulation rates increased

- Number of patients not receiving anticoagulation therapy: pre-clinics 39, post-clinics 14
- Number of patients on NOACs: pre-clinics 0, post-clinics 27
- Number of patients on aspirin only: pre-clinics 156, post-clinics 60

- At the end of each clinic recommendations given to each participating GP practice
  - recorded together with a summary of the discussion with the patient

- Initial findings showed that:
  - 36 additional patients had been added to the AF registers
  - 40 additional people had been anticoagulated
  - Prevalence figures are now highest in the North West
Work 2015/16

• Rationale for work:
  • NICE guidance published in June 2014
  • Numbers changed in 13/14 not high, more to achieve
  • GRASP tool now showed 54 expected strokes a year

• Knew that registers were up to date

• Aim: increase anticoagulation and better management of AF
### Data 15/16

<table>
<thead>
<tr>
<th>Baseline Search (15/20 practices)</th>
<th>Excluded as OAC stopped due to previous bleed/other c/i</th>
<th>Excluded in first phase due to on antiplatelet plus CVD</th>
<th>Excluded due to Chads vasc score (0 or 1 if F)</th>
<th>AF resolved Read code</th>
<th>Dementia/EOL diagnosis</th>
<th>Excluded due to severe alcoholism</th>
<th>Currently under investigat’n with specialist</th>
<th>To offer choice OAC - men with Chads vasc = 1</th>
<th>To offer choice warfarin/NOAC</th>
<th>To offer NOAC OR Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>893</td>
<td>165</td>
<td>136</td>
<td>109</td>
<td>69</td>
<td>87</td>
<td>10</td>
<td>31</td>
<td>25</td>
<td>117</td>
<td>15</td>
</tr>
</tbody>
</table>
Case studies

1. New AF diagnosed by specialist, preserved LV function
   - CHA2DS2 VASc = 5 (risk of stroke 6.7%)
   - Has bled = 3 (risk of bleed 3.7%)
   - MI 1993
   - IHD since 1994
   - Female, age 91
   - Start warfarin or NOAC?
     - Stop aspirin? (risk of bleed combination aspirin and warfarin = 5.1%, risk of bleed warfarin alone = 1.9%)

2. New atrial flutter, waiting further investigations, no other medical history of note
   - Age 61
   - Female
   - Start warfarin or NOAC?

3. AF diagnosed by ECG, 2014, on aspirin
   - CHA2DS2 VASc = 1 (risk of stroke 1.3%)
   - Has bled = 3 (risk of bleed 3.7%) – alcohol, BP and aspirin
   - Age 62
   - Male
So...

- 893 people identified
- 152 to ‘straightforwardly’ offer OAC = 17%

BUT

- 136 people with CVD already on antiplatelet
  - Problem - no agreed guidance to follow, apart from EHA version 4
- Other groups to agree management – no clear current guidance
- Most people will decline an OAC, say 50%

16-30% of cohort likely to start anticoagulant = approx 220 people

- How do we encourage people?
- How do we manage the risk – both of prescribing or not prescribing?
Further work to do in 2015/16

• Ensuring NPSA warfarin guidance is actioned
• So that TTR <65% can be easily calculated
  • Also data can be requested from the Fylde Coast ADAS service

• Reviewing ‘AF probable’ from GRASP AF
• OACs for other indications
• Embedding pulse checks in practice templates
• Liaising with community pharmacies to ensure patients are aware of OACs and practice systems
• Annual review and follow up for anyone on a NOAC
Summary:

Lots of progress

People are very reluctant to take OACs and need clear information and reassurance

Time spent face to face and access to further advice is essential

Common ground for managing complex people still needs to be agreed

THANKS FOR LISTENING ANY QUESTIONS?
How can we use technology to improve identification and management of atrial fibrillation?

Dr. Umesh Chauhan
Using Technologies to improve identification and manage Atrial Fibrillation

Dr Umesh Chauhan
GP
26th June 2015
Background
Incidence rate per 1,000 person years

- **Women**
- **Men**

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-59</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>60-69</td>
<td>1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>70-79</td>
<td>4.0</td>
<td>8.0</td>
</tr>
<tr>
<td>80-89</td>
<td>8.0</td>
<td>12.0</td>
</tr>
</tbody>
</table>

*Data extracted from* http://www.medicine.ox.ac.uk/bandolier/booth/AF/incafu.png
AF Prevalence East Lancashire
Pre-existing Illness before Stroke
2013-2014

Southport and Formby District General
Blackpool Victoria Hospital
Royal Blackburn Hospital
Royal Preston Hospital
Furness General Hospital
Royal Lancaster Infirmary

Hypertension before stroke
Atrial Fibrillation (AF) before stroke
If AF before stroke, on anticoagulant medication:
Illness Preceding Stroke at ELTH

- Hypertension before Stroke:
  - ELHT Q1 2014: 50%
  - ELHT Q2 2014: 50%

- AF before Stroke:
  - ELHT Q1 2014: 10%
  - ELHT Q2 2014: 10%

- If AF before stroke, on anticoagulant medication:
  - ELHT Q1 2014: 60%
  - ELHT Q2 2014: 60%
NICE Hypertension guidelines 2011

2. Because automated devices may not measure blood pressure accurately if there is pulse irregularity (for example, due to atrial fibrillation), palpate the radial or brachial pulse before measuring blood pressure. If pulse irregularity is present, measure blood pressure manually using direct auscultation over the brachial artery. [new 2011]

Makes ABPM and HBPM use rather difficult for this population group

Key research recommendations

1. Which automated blood pressure monitors are suitable for people with hypertension and atrial fibrillation?
Watch BP Home
Atrial Fibrillation

Atrial fibrillation: the management of atrial fibrillation

Clinical guideline

Methods, evidence and recommendations

June 2014
**Diagnosis and investigations**

**Look for AF by OPPORTUNISTIC CASE FINDING**
- Take the pulse in those with:
  - Breathlessness
  - Palpitations
  - Syncope/dizziness
  - Chest discomfort
  - Stroke/TIA
- Do NOT screen asymptomatic populations (evidence shows no benefit).

AF may also be detected as an incidental finding on clinical examination.

---

**Irregular pulse: AF suspected: do ECG**

If paroxysmal AF suspected: do a 24h ECG OR use an event recorder ECG in those who have infrequent episodes (less than daily).

---

**ECG confirms AF or flutter**

<table>
<thead>
<tr>
<th>Patient education</th>
<th>Stroke prevention/bleeding risk assessment</th>
<th>Rate/rhythm control</th>
<th>Bloods? Echo? Referral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensure patient has up to date information on AF including: cause, effects, possible complications, management (rate/rhythm control, stroke prevention) and support networks. See Useful websites box for some useful patient sites.</td>
<td>Assess stroke risk using CHA2DS2-Vasc (preferred to CHADS2). AND Assess bleeding risk using HASBLED.</td>
<td>Rate control is treatment of choice for majority. Rhythm control may be indicated if: AF with reversible cause (e.g., pneumonia)? Heart failure thought to be caused mainly by AF? New onset AF? (NICE don’t define ‘new’, but they are trying to identify those with a good story for recent onset, e.g., ‘I suddenly got these dreadful palpitations’. )</td>
<td>Bloods: NICE do not recommend any blood tests. Most people would check FBC, renal and thyroid function as a minimum. Echo: do NOT routinely do echo. Do echo only if result will change management (see criteria below). Referral to specialist: routine referral not needed. Refer promptly if treatment fails to control symptoms.</td>
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Irregular pulse: AF suspected: do ECG

If paroxysmal AF suspected: do a 24h ECG OR use an event recorder ECG in those who have infrequent episodes (less than daily).
Opportunistic Screening

general practice remain asymptomatic. However, as AF commonly occurs in association with risk factors, such as hypertension, diabetes and ischaemic heart disease, opportunistic assessment of such patients for the presence of AF may be prudent, especially since such patients are frequently seen for check-ups in primary care.
Irregular pulse: AF suspected: do ECG

If paroxysmal AF suspected: do a 24h ECG OR use an event recorder ECG in those who have infrequent episodes (less than daily).

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- AF with reversible cause (e.g. pneumonia)?  
- Heart failure thought to be caused mainly by AF?  
- New onset AF? (NICE don't define 'new', but they are trying to identify those with a good story for recent onset, e.g. 'I suddenly got these dreadful palpitations'.) | · Bloods: NICE do not recommend any blood tests. Most people would check FBC, renal and thyroid function as a minimum.  
· Echo: do NOT routinely do echo. Do echo only if result will change management (see criteria below).  
· Referral to specialist: routine referral not needed. Refer promptly if treatment fails to control symptoms. |
Risk Factors for......

Developing AF
• Hypertension
• IHD
• Heart Failure
• Diabetes
• Thyrotoxicosis
• Alcohol
• Age
• BMI

Developing Stroke
• Hypertension
• Heart Failure
• Diabetes
• 50 years of observation (202 417 person-years)
• Age adjusted prevalence quadrupled from 20.4 to 96.2 cases per 1000 person years in men (13.7 to 49.9 in women)
• Incidence increased from 3.7 to 13.4 new cases per 1000 person years in men (2.8 to 8.6 in women)
• Change in modifiable risk factors:
  • Hypertension and its treatment
  • Diabetes
  • Obesity
The SAFE Study

• **PARTICIPANTS:** Patients aged 65 years and over.

• **INTERVENTIONS:** GPs and practice nurses in the intervention practices received education on the importance of AF detection and ECG interpretation. Patients in the intervention practices were randomly allocated to systematic (n = 5000) or opportunistic screening (n = 5000).

• **MAIN OUTCOME MEASURES:** AF detection rates in systematically screened and opportunistically screened populations in the intervention practices were compared with AF detection rate in 5000 patients in the control practices.

• **RESULTS:** Both systematic and opportunistic screening of people over the age of 65 years are more effective than routine practice (OR 1.57, 95% CI 1.08 to 2.26 and OR 1.58, 95% CI 1.10 to 2.29, respectively). The number needed to screen in order to detect one additional case compared to routine practice was 172 (95% CI 94 to 927) for systematic screening and 167 (95% CI 92 to 806) for opportunistic screening.

**CONCLUSIONS:** The only strategy that improved on routine practice was opportunistic screening, model-based analyses indicated that there was a probability of approximately 60% of annual opportunistic screening being cost effective.

AliveCor
Welcome, Dr Umesh Chauhan

Rest metal electrodes on fingertips as illustrated below.

25 mm/s  10 mm/mV  Enhanced Filter
ECG Analysis
Print
Email
PDF
Cancel
AF Detection Evaluation

• Part funded by ASHN NWC and East Lancashire CCG
• Evaluation by UCLAN

• Aim: To evaluate the feasibility of opportunistic AF screening using MyDiagnostick in general practice, community pharmacy and nursing home settings in East Lancashire.
Objectives

• To evaluate the uptake of MyDiagnostick use for opportunistic screening for AF in general practice, community pharmacy and nursing home settings.

• To analyse the costs and resources required to implement opportunistic AF screening in primary care settings.

• To evaluate patient and carer understanding and acceptability of opportunistic AF screening in primary care settings.

• To evaluate the views of health care staff about the usability of the system, their confidence and training needs in relation to opportunistic AF screening in primary care settings.
FACE
HAS THEIR FACE FALLEN ON ONE SIDE? CAN THEY SMILE?

ARMS
CAN THEY RAISE BOTH ARMS AND KEEP THEM THERE?

SPEECH
IS THEIR SPEECH SLURRED?

TIME
TO CALL 999 IF YOU SEE ANY SINGLE ONE OF THESE SIGNS

WHEN STROKE STRIKES, ACT F.A.S.T.
Number of registered Patients in East Lancashire over 65 years

<table>
<thead>
<tr>
<th>Locality</th>
<th>No. practices</th>
<th>No. of patients (over 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossendale</td>
<td>9</td>
<td>11701</td>
</tr>
<tr>
<td>Burnley</td>
<td>16</td>
<td>16437</td>
</tr>
<tr>
<td>Ribblesdale</td>
<td>4</td>
<td>7905</td>
</tr>
<tr>
<td>Hyndburn</td>
<td>17</td>
<td>12892</td>
</tr>
<tr>
<td>Pendle</td>
<td>13</td>
<td>15273</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>59</strong></td>
<td><strong>64208</strong></td>
</tr>
</tbody>
</table>
Number of Care homes and beds across East Lancashire

<table>
<thead>
<tr>
<th>Locality</th>
<th>No. of Care Homes</th>
<th>No. of beds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossendale</td>
<td>20</td>
<td>706</td>
</tr>
<tr>
<td>Burnley</td>
<td>27</td>
<td>883</td>
</tr>
<tr>
<td>Ribblesdale</td>
<td>9</td>
<td>305</td>
</tr>
<tr>
<td>Hyndburn</td>
<td>21</td>
<td>726</td>
</tr>
<tr>
<td>Pendle</td>
<td>21</td>
<td>714</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>98</strong></td>
<td><strong>3334</strong></td>
</tr>
</tbody>
</table>
Pharmacies

- Over a 100 pharmacies in East Lancashire
- 5 community pharmacies in East Lancashire will take part in the first instance
- Detection will be targeted at those most at risk of AF:
  - Patients over the age of 65 years of age
  - With at least one underlying risk factor (diabetes, hypertension, CHD, heart failure for example).
  - Not known to have AF or on treatment for AF.
# Results from one Practice (10 months)

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Practice Population</strong></td>
<td>6,400</td>
</tr>
<tr>
<td><strong>AF Prevalence</strong></td>
<td>2%</td>
</tr>
<tr>
<td><strong>Number of Patients</strong></td>
<td></td>
</tr>
<tr>
<td>offered test</td>
<td>404</td>
</tr>
<tr>
<td><strong>Number of negative</strong></td>
<td></td>
</tr>
<tr>
<td>Results</td>
<td>380</td>
</tr>
<tr>
<td><strong>Number of Positive</strong></td>
<td></td>
</tr>
<tr>
<td>Results (Required ECG)</td>
<td>14</td>
</tr>
<tr>
<td><strong>Number Diagnosed</strong></td>
<td></td>
</tr>
<tr>
<td>with AF</td>
<td>3</td>
</tr>
</tbody>
</table>
Potential for further development

• Patient self monitoring and increased monitoring within the community
Thank you

Any Questions?

umesh.chauhan@nhs.net
Atrial Fibrillation and Stroke Prevention

Dr Shuja Punekar
Consultant Cerebrovascular Physician
Warrington Hospitals
Atrial Fibrillation
And
Stroke Prevention

Shuja Punekar
Consultant Cerebrovascular Physician
Hon Senior Lecturer, Manchester Medical School
Disclosure: I have received Speaker-fee and sponsorship from Boehringer-Ingelheim and BMS/Pfizer
• Hospitals - a magnet for patients with AF
• What proportion of Stroke patients have AF
  – And how many are anticoagulated before their Stroke
• Anticoagulation strategies
• NOACs - safety
• Way forward
63 year old man – seen in a Hospital Clinic – AF on ECG

Not anti-coagulated

Admitted 2012 with Cardio-embolic Right Cerebral Infarct

Thrombolysed with minimal benefit

Discharged with a severe disability
Atrial Fibrillation

How Common in Hospitals?
In Acute Medical Admissions?
Approximate Prevalence of AF by age groups

- 65+: 5%
- 75+: 10%
- 85+: 20%
Prevalence of AF in Acute Medical admissions in Preston

- 500 consecutive acute medical admissions at RPH were screened for AF
  - 50 years of age or over between 11 May and 1 June 2010

- 102 had AF; Prevalence = 20.4%
  - 59% were F and 41% M
  - Mean age was 78

Lucy Freeman, Shuja Punekar. 2010
Awarded ‘Best Student Oral Presentation’ at the UK Stroke Conference Nov/Dec 2010
<table>
<thead>
<tr>
<th>Total No of patients</th>
<th>55</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>85 years</td>
</tr>
<tr>
<td>Male/Female</td>
<td>25/30 45%/55%</td>
</tr>
<tr>
<td>Patients with AF</td>
<td>22 40%</td>
</tr>
<tr>
<td>Patients with AF &amp; CHADS2 score of 2 or more</td>
<td>19 86.4%</td>
</tr>
</tbody>
</table>

40% of hospitalised elderly (75+yrs) were in AF and nearly 90% of those had a CHADS2 score of 2 or above

Zobia Ahmed & Shuja Punekar; 2012
What Proportion of Patients with Acute Stroke have AF

How many are anticoagulated
A retrospective audit of all Ischaemic Stroke (495) patients from 2012 at RPH:

- 22% of all IS patients have AF & 30% of 75yrs or above have AF
- Only 12% of all patients were anticoagulated before their Stroke

Matt Wix and Shuja Punekar, 2013
AF in Care Homes

Study Carried out in Care homes in Preston (May-June 2011)

Overall Break-Down of Residents Including Number with AF and Status of Anticoagulation

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of Residents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cohort</td>
<td>231</td>
</tr>
<tr>
<td>Residents with AF</td>
<td>44 (19%)</td>
</tr>
<tr>
<td>Correct Anticoagulant Prescribed</td>
<td>17 (39%)</td>
</tr>
<tr>
<td>No Anticoagulant Prescribed</td>
<td>14 (32%)</td>
</tr>
<tr>
<td>Incorrect Anticoagulant Prescribed</td>
<td>13 (29%)</td>
</tr>
</tbody>
</table>

McCrory S, Punekar SN; 2011
Estimating Stroke Risk in AF & Bleeding Risk with Anticoagulation
Assessment of Cardio-embolic and bleeding risks

<table>
<thead>
<tr>
<th>CHA₂DS₂-VASc</th>
<th>Score</th>
<th>HAS-BLED</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
<td>Hypertension (systolic blood pressure &gt; 160 mm Hg)</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>Abnormal renal and liver function* (1 point each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Age ≥75 y</td>
<td>2</td>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
<td>Bleeding tendency/predisposition*</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/TE</td>
<td>2</td>
<td>Labile INRs (if on warfarin)*</td>
<td>1</td>
</tr>
<tr>
<td>Vascular disease (prior MI, PAD, or aortic plaque)</td>
<td>1</td>
<td>Elderly (eg, age ≥65 y)</td>
<td>1</td>
</tr>
<tr>
<td>Aged 65 to 74 y</td>
<td>1</td>
<td>Drugs or alcohol (1 point each)*</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Sex category (ie, female sex)</td>
<td>1</td>
<td>Maximum score</td>
<td>9</td>
</tr>
<tr>
<td>Maximum score</td>
<td>9</td>
<td>Maximum score</td>
<td>9</td>
</tr>
</tbody>
</table>
Risk of Intracranial haemorrhage rises steeply for INRs over the therapeutic range (Q J Med 2011; 104:747–760)
Anticoagulation related IC haemorrhages can grow rapidly and be fatal
One-year survival rate after ICH was 35.2% among warfarin users vs 67.9% among nonusers. P<0.001

Anticoagulation related ICH and 30 day mortality in RPH, Preston, 2012 - 2014

p = ns

<table>
<thead>
<tr>
<th></th>
<th>Total patients</th>
<th>30 day mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoag</td>
<td>4 (29%)</td>
<td>14</td>
</tr>
<tr>
<td>Non-Anticoag</td>
<td>39 (33%)</td>
<td>118</td>
</tr>
</tbody>
</table>

Sarah Manohar & Shuja Punekar; June 2014
How good are we in achieving target INR in patients on warfarin
In most RCTs we see ‘Time in Therapeutic Range’ (TTR) to be between 60 – 70 % as demonstrated here for AF patients on oral anticoagulation.
Lancs Teaching Hospitals
Anticoagulation Clinic Audit  June 2014

Proportion of patients in therapeutic range over time

- 83.5% of patients 65% or more time in range
- 72.5% of patients 75% or more time in range
- 60.6% of patients 85% or more time in range
- 36.5% of patients 95% or more time in range

Taher Esmailji & Shuja Punekar
Lancs Teaching Hospitals
Anticoagulation Clinic Audit  June 2014

Number of patients with high INRs

<table>
<thead>
<tr>
<th>INR Range</th>
<th>Under 65</th>
<th>65 and Above</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 or &gt;</td>
<td>7</td>
<td>59</td>
</tr>
<tr>
<td>5 or &gt;</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>6 or &gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7 or &gt;</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>8 or &gt;</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>9 or &gt;</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>10 or &gt;</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Taher Esmailji & Shuja Punekar
AF
Anticoagulation Strategies
In
Primary and Secondary
Stroke Prevention
NNT

- NNT to prevent 1 stroke per year of anticoagulation therapy in secondary prevention (ARR: 8.5%) = 12
  
  NNT for Secondary Prevention = 12

  NNT for Primary Prevention = 37

- NNT in primary prevention = 37
All patients with TIA in AF to be treated as high risk

Patients with TIA in AF should be anticoagulated with an agent that has rapid onset in the TIA clinic once intracranial bleeding has been excluded and if there are no other contra-indications.
Patients with TIA in AF should be anticoagulated with:
1. Outpatient Warfarinisation - therapeutic in 4 weeks
2. Daily Low Mol. Wt. Heparin Injections + commence Warfarin - daily district nurse visits for up to 2 weeks
3. Commence a NOAC in clinic – therapeutic in 2 hours
How soon should we start anticoagulation Post-Cardioembolic Stroke?

RCP 2012 Stroke Guidelines

In the case of patients with acute cardioembolic stroke, there is concern that anticoagulation may increase the risk of haemorrhagic transformation, and a delay for an arbitrary 2 week period is recommended.
20/05/2015
Pre-thrombolysis
Admitted with
Expressive Dysphasia
Excellent Recovery
With Thrombolysis

25/05/2015
Post-thrombolysis
Small left-frontal infarct

02/06/2015
Recurrent Stroke
In Less than 2 weeks
Right MCA Infarct
Has AF – not yet anticoagulated

Mrs JB, 84 yrs, RIP after 2^{nd} Stroke
Mr BG, 75yrs, discharged 10\textsuperscript{th} Nov 2014 following a Left Cerebral (MCA) Infarct

Known AF – Stopped Warfarin for 1 week for a procedure

Recommenced Warfarin – 3\textsuperscript{rd} Nov 2014

Left MCA Infarct with exp dysphasia and RUL weakness (NIHSS = 7) – 6\textsuperscript{th} Nov 2014

INR = 1.1 on admission

Delayed onset of therapeutic effect with Warfarin to blame
Thousands of strokes in people with common heart rhythm disorder are avoidable, says NICE

Updated guidance highlights the need to ensure people with atrial fibrillation (AF) are offered the right treatments to reduce their chance of dying from strokes

View the guidance
Read the news

NICE News release 18th June 2014
AF NICE Guidelines 2014

• Use the CHA2DS2-VASc stroke risk score to assess stroke risk in people with AF

• Use the HAS-BLED score to assess the risk of bleeding in people who are starting or have started anticoagulation

• Do not offer aspirin mono-therapy solely for stroke prevention to people with atrial fibrillation
Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist.

Consider anticoagulation for men with a CHA2DS2-VASc score of 1.
- Take the bleeding risk into account.

Offer anticoagulation to people with a CHA2DS2-VASc score of 2 or above, taking bleeding risk into account.

Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences.
AF NICE Guidelines 2014

• If poor anticoagulation control cannot be improved, evaluate the risks and benefits of alternative stroke prevention strategies and discuss these with the patient.

• Poor anticoagulation
  – 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%.
The way forward

• Improve the recognition of AF
  • In primary as well as secondary care
  • Too many AF patients are discharged from hospitals without anticoagulation

• Improve the Uptake of anticoagulation
  • Patient and Clinician awareness and education
  • Choose the right agent

• Improve the speed of anticoagulation
  • Warfarin clinics routinely take at least 2 weeks to achieve therapeutic INR for outpatients
  • NOACs are a reasonable choice in TIA with AF for immediate anticoagulation

• Make anticoagulation safer
  • Stricter monitoring of both Warfarin and NOAC patients
Thank you
Morning Break
Approaches to anti-coagulation and management of atrial fibrillation across Primary Care in Lancashire

Dr Mammen Ninnan
GP and Strategic Clinical Network Lead for atrial fibrillation in Lancashire
How well is stroke prevention in AF achieved across Lancashire

• GRASP-AF audits run across the county shows
  
  ▪ 80-85% AF patients have CHADSVASc score > 1
  ▪ significant proportion of patients ~ 30% still on Aspirin or without any anticoagulant
Patients not on anticoagulation – January 2015

- NHS Blackpool: 31.1% (100%)
- NHS Blackburn with Darwen: 38.6% (64.2%)
- NHS Chorley & South Ribble
- NHS East Lancashire: 31.4% (1.69%)
- NHS Fylde & Wyre: 32.9% (100%)
- NHS Greater Preston: 39.6% (12.1%)
- NHS Lancashire North: 32.4% (100%)
- NHS West Lancashire: 39.8% (100%)
• Personalised package of care
• Aspirin NOT to be used as monotherapy for stroke prevention in AF
• CHA$_2$DS$_2$-VASc score to be used for risk scoring and HASBLED score for bleeding risk
• Any of the 4 available OAC can be used with emphasis on patient informed choice
• Not to withhold anticoagulation solely because of risk of falls

NICE guidance
• 4 anticoagulant agents currently available – warfarin, dabigatran, rivaroxaban and apixaban.
• Self-monitoring of warfarin is an option recommended by NICE, but with cost and resource implications.
• NOACs increasingly prescribed by clinicians, but with variable follow up strategy

Approaches to anticoagulation
AF subgroups to target

- Asymptomatic patients with AF
  - Improve detection strategies both in community and in hospitals – make every patient encounter COUNT
- Patients with diagnosed AF who are not on anticoagulation
  - Strategies to improve audit and review of all AF patients
  - Education and training to the whole clinical team
- Patients on warfarin with suboptimal ‘Time in therapeutic range’
  - Quality targets for anticoagulation providers
  - Protocols for dealing with poor warfarin control
Primary & Secondary Prevention Gap Analysis – Lancashire & South Cumbria

<table>
<thead>
<tr>
<th></th>
<th>AF and Hypertension identification and diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AF detection and diagnosis</td>
</tr>
<tr>
<td></td>
<td>Hypertension detection and diagnosis</td>
</tr>
<tr>
<td></td>
<td>Mandatory annual pulse rhythm check for pts &gt;65yrs or with LTC</td>
</tr>
<tr>
<td></td>
<td>Use of GRASP/other casefinder and care management tools</td>
</tr>
<tr>
<td></td>
<td>Every patient contact counts; manual pulse, weight and BP checks (all healthcare settings)</td>
</tr>
<tr>
<td></td>
<td>Accurate recording and coding of patient diagnosis to enable effective treatment and monitoring</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NHS Health Checks Pts Offered / Pts Received</th>
<th>Offered</th>
<th>Received</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF and Hypertension identification and diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension detection and diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandatory annual pulse rhythm check for pts &gt;65yrs or with LTC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of GRASP/other casefinder and care management tools</td>
<td></td>
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<td>Every patient contact counts; manual pulse, weight and BP checks (all healthcare settings)</td>
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<td></td>
</tr>
<tr>
<td>Accurate recording and coding of patient diagnosis to enable effective treatment and monitoring</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Green indicates little/no gap between current practice and what's included in the spec, this may be due to initiatives, processes, pathways, services etc. already in place.
Amber indicates some work to do to achieve the spec but may be building on initiatives etc. already in place.
Red indicates a significant amount of work to do to achieve the spec in this area, this may be due to poor quality or no existing initiatives etc.
White indicates information not known or not provided.
## Primary & Secondary Prevention Gap Analysis – Lancashire & South Cumbria

<table>
<thead>
<tr>
<th>Training &amp; Education</th>
<th>Awareness &amp; Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Care staff - Stroke prevention</strong></td>
<td><strong>Nursing home staff trained to regularly check BP, temp, pulse rhythm</strong></td>
</tr>
<tr>
<td>Green</td>
<td>Red</td>
</tr>
<tr>
<td>Amber</td>
<td>Red</td>
</tr>
<tr>
<td>Red</td>
<td>Red</td>
</tr>
<tr>
<td>White</td>
<td>White</td>
</tr>
</tbody>
</table>

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## Primary & Secondary Prevention Gap Analysis – Lancashire & South Cumbria

<table>
<thead>
<tr>
<th>Condition management</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF management (anticoag prescribing)</td>
</tr>
<tr>
<td>AF management (access to anticoag services)</td>
</tr>
<tr>
<td>Hypertension management (medication)</td>
</tr>
<tr>
<td>Stroke patients - Review of health, social care and secondary prevention needs in primary care 6 weeks post discharge</td>
</tr>
<tr>
<td>TIA patients - Risk factor review in primary care 1 month post diagnosis</td>
</tr>
<tr>
<td>Stroke &amp; TIA patients - annual secondary prevention/risk factor review in primary care</td>
</tr>
</tbody>
</table>

Green indicates little /no gap between current practice and what's included in the spec, this may be due to initiatives, processes, pathways, services etc. already in place.

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Red indicates a significant amount of work to do to achieve the spec in this area, this may be due to poor quality or no existing initiatives etc.

White indicates information not known or not provided.
Suspect a stroke? Act FAST and call 999.

FAST

Facial weakness Arm weakness Speech problems Time to call 999
Genotype guided dosing for warfarin

Dr Richard Turner
North West England MRC Fellow in
Clinical Pharmacology & Therapeutics
University of Liverpool
Genotype-Guided Warfarin Dosing

Dr Richard Turner
North West England MRC Fellow in Clinical Pharmacology & Therapeutics

On behalf of: Prof Sir Munir Pirmohamed
David Weatherall Chair of Medicine
Department of Molecular and Clinical Pharmacology
University of Liverpool
Warfarin

- Number of users UK: 600,000
- Dose (mg) range per day: 0.5-20
- Fold variability in dose: 40
- Major bleeding rate per 100-person years: 2.6
- Ranking in ADR list: 3

Approved for human use in 1954
Warfarin

γ-glutamyl carboxylase

VKORC1

Cotting factors II, VII, IX, X

Metabolites

Vitamin K

Warfarin

R

CYP1A2

CYP2C9

CYP3A4

S

S
Variation in Dose Requirements

UK prospective cohort data

<table>
<thead>
<tr>
<th>INR</th>
<th>Incidence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>4.11</td>
</tr>
<tr>
<td>2.1-3.0</td>
<td>3.78</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>15.78</td>
</tr>
<tr>
<td>&gt;4.1</td>
<td>99.26</td>
</tr>
</tbody>
</table>

Hylek et al, 2007
Oral anticoagulation: a critique of recent advances and controversies

Munir Pirmohamed¹,², Farhad Kamali³, Ann K. Daly³, and Mia Wadelius⁴

¹ The University of Liverpool, Liverpool L69 3BX, UK
² Royal Liverpool and Broadgreen University Hospital National Health Service (NHS) Trust, Prescot Street, Liverpool L7 8XP, UK
³ Newcastle University, Newcastle upon Tyne NE2 4HH, UK
⁴ Uppsala University, 751 85 Uppsala, Sweden

Trends in Pharmacological Sciences, March 2015, Vol. 36, No. 3

Clinical and environmental factors

- Age
- Body mass index
- Gender
- Enzyme inducer interactions
- Enzyme inhibitor interactions
- Other interacting medications
- Comorbid conditions
- Nutritional status
- Adherence
- Diet
- Smoking
- Alcohol

Genetic factors

- VKORC1 (25%)
- CYP2C9 (15%)
- CYP4F2 (1%)
GWAS Warfarin Mean Weekly Dose
(UK Prospective Cohort; n=714)

Total = 57.9%
Age: 11.2%
Height 3.56%
Weight: 5.98%
Sum of interacting meds: 2.2%
VKORC1: 25.61%
CYP2C9: 16.65%
CYP4F2: 0.49%
Pharmacogenetic-Based Dosing: Warfarin Randomised Controlled Trial

- FP7 sponsored EU trials
- 454 patients
  - 226 in genotype arm
  - 228 in standard care arm
- Point of Care test for genotyping

European Union Pharmacogenetics of AntiCoagulant Therapy
Warfarin Dosing – Standard Clinical Care

Thrombotic disorder
- Clinical decision

Loading Dose
- 3 doses
- 10,5,5mg
- 5,5,5mg (over 75 years)

Day 4
- INR checked
- Dosing – using clinical practice

Day 6 onwards
- INR checked
- Dose adjusted according to INR – local clinical practice
The Genetic Warfarin Dosing Pathway

Thrombotic disorder
- Clinical decision

Loading dose algorithm

Loading Dose
- Individualised
- Algorithm developed with genetic and clinical factors

Dose revision algorithm

Day 4
- INR checked
- Dosing – individualised based on clinical and genetic factors

Usual clinical care

Maintenance
- INR checked
- Dose adjusted according to INR by computer software
A Randomized Trial of Genotype-Guided Dosing of Warfarin

<table>
<thead>
<tr>
<th>Genotyped arm</th>
<th>Standard dosing (control) arm</th>
<th>Adjusted Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>%TTR</td>
<td>%TTR</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ITT ANALYSIS (n= 211 vs 216)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>67.4%</td>
<td>60.3%</td>
<td>7%</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td><strong>PER-PROTOCOL (n=166 vs 184)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>68.9%</td>
<td>62.3%</td>
<td>6.6%</td>
<td>P=0.001</td>
</tr>
</tbody>
</table>

**PRIMARY OUTCOME MEASURE**: Percent time within therapeutic INR range 2.0-3.0 (TTR) during 12 weeks following the initiation of warfarin therapy.
### Differences in %Time in Therapeutics Range According to Treatment Month

<table>
<thead>
<tr>
<th></th>
<th>Genotyped arm</th>
<th>Control arm</th>
<th>Difference (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adjusted mean</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(95% CI) % Time in range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>weeks 1-4</strong></td>
<td>55.72</td>
<td>46.96</td>
<td>8.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(52.12, 59.33)</td>
<td>(43.36, 50.56)</td>
<td>(4.39, 13.14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>weeks 5-8</strong></td>
<td>74.36</td>
<td>64.19</td>
<td>10.17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(69.57, 79.16)</td>
<td>(59.40, 68.98)</td>
<td>(4.36, 15.99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>weeks 9-12</strong></td>
<td>75.47</td>
<td>74.11</td>
<td>1.36</td>
<td>0.607</td>
</tr>
<tr>
<td>(71.21, 79.72)</td>
<td>(69.81, 78.40)</td>
<td>(-3.84, 6.57)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Differences Between Genotyped-Guided Group and Control Group

International Normalized Ratio

Time in Therapeutic Range
Secondary Outcomes

Time to Reach Therapeutic INR

- Genotyping reduced risk of, and % time above, an INR≥ 4.0
- Genotyping reduced the number of dose adjustments

Time to Reach Stable Dose

- HR 1.43 (95% CI 1.17, 1.76) P<0.001
- HR 1.40 (95% CI 1.12, 1.74) P<0.001
A Pharmacogenetic versus a Clinical Algorithm for Warfarin Dosing

Stephen E. Kimmel, M.D., Benjamin French, Ph.D., Scott E. Kasner, M.D., Julie A. Johnson, Pharm.D., Jeffrey L. Anderson, M.D., Brian F. Gage, M.D., Yves D. Rosenberg, M.D., Charles S. Eby, M.D., Ph.D., Rosemary A. Madigan, R.N., M.P.H., Robert B. McBane, M.D., Sherif Z. Abdel-Rahman, Ph.D., Scott M. Stevens, M.D., Steven Yale, M.D., Emile R. Mohler III, M.D., Margaret C. Fang, M.D., Vinay Shah, M.D., Richard B. Horenstein, M.D., Nita A. Limdi, Pharm.D., Ph.D., James A.S. Muldowney III, M.D., Jaspal Gujral, M.B., B.S., Patrice Delafontaine, M.D., Robert J. Desnick, M.D., Ph.D., Thomas L. Ortel, M.D., Ph.D., Henny H. Billett, M.D., Robert C. Pendleton, M.D., Nancy L. Geller, Ph.D., Jonathan L. Halperin, M.D., Samuel Z. Goldhaber, M.D., Michael D. Caldwell, M.D., Ph.D., Robert M. Califf, M.D., and Jonas H. Ellenberg, Ph.D., for the COAG Investigators*

No difference between genotyped and control arms

Algorithmic strategy
Ethnic heterogeneity
Control arms (Clinical algorithm vs fixed dosing)
Clinical relevance
Ethnic Heterogeneity

- COAG was more heterogeneous (67% white, 27% Black, 6% Hispanic) than EU-PACT (97% Caucasian)
- Black patients did worse in genotype arm than in clinical group (-8% difference)

<table>
<thead>
<tr>
<th>Allele</th>
<th>Location</th>
<th>Frequency</th>
<th>European Caucasians</th>
<th>US Hispanics</th>
<th>African-Americans</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2C9*2</td>
<td>Exon 3</td>
<td>0.10</td>
<td>0.07</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>CYP2C9*3</td>
<td>Exon 7</td>
<td>0.06</td>
<td>0.05</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>CYP2C9*5</td>
<td>Exon 7</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>CYP2C9*6</td>
<td>Exon 5</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>CYP2C9*8</td>
<td>Exon 3</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>CYP2C9*11</td>
<td>Exon 7</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>CYP2C9 rs7089580</td>
<td>Intrinsic</td>
<td>0.24</td>
<td>0.11</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>VKORC1 -1639A</td>
<td>5-UTR</td>
<td>0.40</td>
<td>0.46</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>VKORC1 rs61162043</td>
<td>5-UTR</td>
<td>Unknown</td>
<td>Unknown</td>
<td>0.47</td>
<td></td>
</tr>
</tbody>
</table>
Ethnic Differences in Warfarin Sensitivity

Wright, Clinical Genetics, 2015
Control Arms in the Two Trials

- EU-PACT: fixed dosing which reflects current clinical care
- COAG: clinical algorithm (includes all factors apart from genetics)
- Interpreted as genetics does not add anything over and above clinical factors – some have advocated use of clinical algorithm
- Clinical algorithm has never been tested in a RCT

<table>
<thead>
<tr>
<th>Trial</th>
<th>Time</th>
<th>Genotyped arm</th>
<th>Control arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>%TTR</td>
<td>%TTR</td>
</tr>
<tr>
<td>COAG</td>
<td>4 weeks</td>
<td>45.2</td>
<td>45.4</td>
</tr>
<tr>
<td>EU-PACT</td>
<td>4 weeks</td>
<td>54.6</td>
<td>45.7</td>
</tr>
<tr>
<td>COAG</td>
<td>12 weeks</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>EU-PACT</td>
<td>12 weeks</td>
<td>67.4</td>
<td>60.3</td>
</tr>
</tbody>
</table>
**EU-PACT: Effect of Number of Variants on % Time in Therapeutic Range (TTR)**

<table>
<thead>
<tr>
<th>Total number of variants</th>
<th>Genotyped arm (n=211) %TTR</th>
<th>Control arm (n=216) %TTR</th>
<th>Adjusted Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>61.83</td>
<td>59.31</td>
<td>2.03</td>
<td>0.588</td>
</tr>
<tr>
<td>1</td>
<td>68.56</td>
<td>61.83</td>
<td>7.38</td>
<td>0.005</td>
</tr>
<tr>
<td>2 or more</td>
<td>71.95</td>
<td>57.32</td>
<td>11.05</td>
<td>0.009</td>
</tr>
</tbody>
</table>

**RELY DATA**: a 10% improvement in %TTR leads to a 20% improvement in clinical outcomes
A 10% increase in time out of INR range associated with:

- increased risk of **mortality** (odds ratio (OR) 1.29, p < 0.001)
- Increased risk of **ischaemic stroke** (OR 1.10, p = 0.006) and
- Increased risk of **other thromboembolic events** (OR 1.12, p < 0.001).
Genetics and the clinical response to warfarin and edoxaban: findings from the randomised, double-blind ENGAGE AF-TIMI 48 trial


- wild type for CYP2C9 and VKORC1
- 1-2 variants
- 3-4 variants

“Genotype added information beyond clinical risk scoring”
incremental cost-effectiveness ratios (ICERs) were £6,702 and 253,848 SEK per QALY gained
# Novel Oral Anticoagulants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Apixaban</th>
<th>Dabigatran</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of action</td>
<td>Direct factor Xa inhibitor</td>
<td>Direct thrombin (IIa) inhibitor</td>
<td>Direct factor Xa inhibitor</td>
<td>Direct factor Xa inhibitor</td>
</tr>
<tr>
<td>Oral bioavailability</td>
<td>50%</td>
<td>3–7%</td>
<td>Approximately 60%</td>
<td>10 mg: 80–100%; 20 mg: 66%</td>
</tr>
<tr>
<td>Half-life</td>
<td>8–15 h</td>
<td>12–17 h</td>
<td>8–10 h</td>
<td>5–9 h</td>
</tr>
<tr>
<td>Metabolism and excretion</td>
<td>27% renal, 73% faecal or biliary</td>
<td>80% renal, 20% faecal</td>
<td>33% renal</td>
<td>66% renal, 33% faecal</td>
</tr>
<tr>
<td>Protein binding</td>
<td>87%</td>
<td>35%</td>
<td>40–59%</td>
<td>92–95%</td>
</tr>
<tr>
<td>Time to peak effect</td>
<td>1–3 h</td>
<td>1–3 h</td>
<td>1–2 h</td>
<td>1–3 h</td>
</tr>
<tr>
<td>Antidote</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Coagulation monitoring</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>CYP3A4, P-glycoprotein</td>
<td>P-glycoprotein</td>
<td>CYP3A4, P-glycoprotein</td>
<td>CYP3A4, P-glycoprotein</td>
</tr>
</tbody>
</table>

![Chemical structures of novel oral anticoagulants]
# Advantages and Disadvantages of NOACs

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard doses</td>
<td>Biomarkers for monitoring not well developed</td>
</tr>
<tr>
<td>No monitoring</td>
<td>Are standard doses safe enough?</td>
</tr>
<tr>
<td>Superior or non-inferior to warfarin</td>
<td>Lack of real world experience</td>
</tr>
<tr>
<td>Lower risk of intracranial haemorrhage</td>
<td>Increased risk of GI bleeding</td>
</tr>
<tr>
<td></td>
<td>No antidote</td>
</tr>
<tr>
<td></td>
<td>Costly</td>
</tr>
<tr>
<td></td>
<td>Twice daily dosing (dabigatran, apixaban)</td>
</tr>
</tbody>
</table>
Use of NOACs in England and Wales

Warfarin: Number of prescriptions
August 2011 – 4,358,120  March 2014 – 5,068,593
Summary

- **Genotype-guided warfarin dosing**
  - For genetic-guided warfarin dosing, algorithmic strategies are crucial in determining anticoagulation control
  - EU-PACT dosing strategy – most impact in those with variants
  - Cost effectiveness analysis
  - Implementation study being developed with NWC AHSN

- **Stratification of anticoagulant therapy**
  - NOACs provide choice for prescribers and patients
  - No strategy for choosing which NOAC to use
  - Warfarin still the most commonly used drug
  - In 35-40% of patients with variants, NOACs could be used
Acknowledgements

The University of Liverpool

- Munir Pirmohamed
- B Kevin Park
- Ana Alfirevic
- Maike Lichtenfels
- Dean Naisbitt
- Andrea Jorgensen
- Dyfrig Hughes
- Fabio Miyajima
- Andrew Swales

- Stephane Bourgeois (Sanger Institute)
- Panagiotis Deloukas (Sanger Institute)
- Ed Conley (Farr Institute)
- EU-PACT
- FDA

Funders: MRC
Dept of Health (NHS Chair of Pharmacogenetics)
WT, DH, NIHR, EU-FP7
Introducing the atrial fibrillation commissioning tool-kit

Jeannie Hayhurst
Quality Improvement Lead
Strategic Clinical Network
AF Commissioning Toolkit

Jeannie Hayhurst
Cardiovascular Specialist Nurse
26th June 2015
Tri – partite Stroke Prevention/AF detection and prevention group

- GM, L & SC Strategic Clinical Network
- Academic Health Science Networks
- Public Health England
Purpose

To reduce the incidence and impact of AF related strokes through an holistic approach to stroke prevention
Aims

To improve outcomes and quality of care for patients through the identification of opportunities for improving detection, identification and treatment of AF
Deliverables

- Guidance for CCG’s and practices
- Toolkit for Commissioning of Services
Partnership working - AHSN

- Investigate technology
- Facilitate pilots
- Produce a framework of equipment
- Share stroke prevention education, training, awareness raising & lessons learnt
Partnership working - PHE

- Scope current provision of opportunistic screening/pulse checks
- Provide wider PHE information e.g. NHS Health Checks and other National initiatives
- Devise guidance and recommendations on incentivisation – evidence base
Provide clinical expertise and guidance through Primary Care Clinical Leads and Clinical Support Leads who would, as part of the toolkit:

- Undertake practice level data analysis around AF and anticoagulation in order to identify opportunities for increased identification and treatment of AF and associated risk factors
- Review and develop guidance around anticoagulation
- Identify effective methods of raising awareness of AF
- Identify training and education requirements around AF
- Develop a commissioning toolkit
Contents

• Summary of Recommendations
• The case for change
• Cost impact and benefits
• Expected outcomes
• Data
• Detection and Diagnosis
• Anticoagulation
• Training and Education
• Technologies
• Examples of best practice
AF Association Healthcare Pioneers – Showcasing best practice in AF report

Blackpool’s multidisciplinary approach utilising:

• GRASP – AF
• Pulse check LES
• Training

Resulted in

• AF prevalence ↑ from 1.6% (2011) to 2.24% (2014)
• Warfarin px increased from 40.51% (2011) to 63.27% (2014)