Setting the Stage. What is needed to move the field forward?

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- Research grants from:
  - Boston Scientific, Medtronic, St. Jude
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Why might AF screening be effective?

- Many new screening technologies
- DOACs have made AF treatment easier
- Aging population; AF-stroke is common
- Large amount of AF can be identified.
WHO attributes of a good screening program

- Important health problem
- Available treatment
- Facilities for diagnosis and treatment
- Asymptomatic phase of disease
- Test for condition; acceptable to public
- Natural history understood; agreement on policy
- Cost of case finding balanced with overall costs
- Test should be sensitive
- Screening should be a continuous process
Steps to a successful AF Screening Program

Identify Suitable Population

Identify Suitable Setting

Select best screening tool and system

Stratify risks

Initiate OAC

Maintain OAC

Evaluate outcomes

Engage:

Patients
Communities
Physicians
Governments/payers

Requirements:

Outcomes research
Implementation research
Economic evaluation
Ideal screening strategy: Depends where?

Population
- Older (55+, 65+, 75+)
  - Tradeoff AF incidence with life-years and technology use
- Additional risk factors
  - CHADS-VASc, HAVOC, others
  - Obesity, sleep apnea
- Biomarkers
  - NT-Pro-BNP
  - Echocardiographic parameters
  - Cost/complexity of markers vs. incremental yield?

Setting
- General population
- Family practice
  - Direct link to treatment?
- Pharmacies
- Vaccination clinics
- Community centres
  - Improved patient-engagement and durability of program?
- Others
### Challenges for Specific Setting

**PIAAF Pharmacy; Open Heart 2017**

<table>
<thead>
<tr>
<th>Age Groups (years)</th>
<th>Total N (%)</th>
<th>‘Actionable’ AF N (%)</th>
<th>No AF N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-74</td>
<td>620 (54.8)</td>
<td>11 (1.8)</td>
<td>609 (98.2)</td>
</tr>
<tr>
<td>75-85</td>
<td>422 (37.3)</td>
<td>9 (2.1)</td>
<td>413 (97.9)</td>
</tr>
<tr>
<td>&gt;85</td>
<td>89 (7.9)</td>
<td>7 (7.9)</td>
<td>82 (92.1)</td>
</tr>
</tbody>
</table>

Approximately 50% of patients had a BP > 140/90 at screening
Only 50% of screen-positive patients receiving OAC 3 months later
PIAAF-Pharmacy

- R. Sandhu, U of A; published Heart Open 2017
- Cost/QALY was $375 CAD; published CMAJ Open 2017
- Limitation was poor delivery of OAC (50%)
- Intervention study now ongoing: Pharmacist prescribing
Different Screening Tools
PIIAF-FP: Objectives/Achievements

• Observational study comparing 3 methods of AF screening in the family practice setting
  • R. Quinn, U of Calgary, N=2054
  • Presentation at HRS 2017
  • Single-lead ECG and Automatic BP machine had 72% and 48% fewer false positives (respectively) than manual palpation
  • Newly-identified AF only 0.6%, using a single test in a group of well-run primary care clinics
3 % new AF, total AF prevalence increase >30 %

- Attends screening clinic, n= 7 173
- Declaration of health
- Known AF, n=666 (9.3%)
- Intermittent ECG-recordings 2 weeks
- No AF
- Silent AF, n=218 (3 %)
- No OAC-treatment, n= 149 (2.1%)
- OAC treatment, n=517

Referral to Cardiologist for OAC

Svennberg et al, Circulation 2015
Cost-effectiveness of mass screening for untreated atrial fibrillation using intermittent ECG recording

Mattias Aronsson, Emma Svennberg, Mårten Rosenqvist, Johan Engdahl, Faris Al-Khalili, Leif Friberg, Viveka Frykman-Kull, and Lars-Åke Levin

1Department of Medical and Health Sciences, Centre for Medical Technology Assessment, Linköping University, SE-581 83 Linköping, Sweden; 2Karolinska Institutet, Department of Clinical Science, Cardiology Unit, Danderyd University Hospital, Stockholm, Sweden; 3Department of Medicine, Halland Hospital, Halmstad, Sweden; and 4Stockholm Heart Centre, Stockholm, Sweden

- 8 fewer strokes/1000 screened
- 12 QALYs / 1000 screened
- € 4313/QALY
Value of combined screening

Possible synergies:
- HTN
- Diabetes
- Influenza vaccine
- Polypill

- Improved efficiency, reduce costs
- Increase acceptability in primary care
Current Challenges for AF Screening

- Stroke prevention is assumed/modelled, not measured
  - Government agencies, high-impact journals demanding more…
- Screening strategy must be adapted for each country and setting
- Some difficulties translating AF detection into delivery of stroke prevention therapy
  - particularly in community settings
Rate of detection in ICM arm was 30.0% vs 3.0% in control arm
NAVIGATE-ESUS Trial Design

Prospective, randomized, double-blind, active-comparator, event-driven, superiority, phase III study

Patients with recent ischemic stroke and
1. visualized by brain CT or MRI that is not lacunar (subcortical infarct ≤1.5 cm)
2. absence of cervical carotid atherosclerotic artery stenosis > 50% or occlusion
3. no atrial fibrillation after ≥ 24 hours cardiac rhythm monitoring
4. no intra-cardiac thrombus on transthoracic echocardiography
5. no other specific etiology for cause of stroke (eg, arteritis, dissection, migraine/vasospasm, drug abuse)

Age ≥ 50 years

~460 sites in 31 countries

Target RRR 30%; superiority w/ 90% power α=0.05
Enrollment ~24 months; minimum treatment ~6 months; study duration ~36 months
Estimated mean treatment duration 6 - 24 months;

\[ N \sim 7,000 \]

Rivaroxaban 15 mg od \( n \sim 3,500 \)
ASA 100 mg od \( n \sim 3,500 \)

Day 1
Randomization

Efficacy Cut-off Date
30±7 days
EOS

1 month post study drug observation period

Randomization 7 days to 6 month after acute ESUS

Two substudies:

- MRI substudy assessing covert strokes (1000 participants)
- Biomarker / genetics substudy to identify biomarkers linked with ESUS, recurrent stroke and treatment response

7000 patients at 460 sites in 31 countries; 450 primary events; expected event rate 3.8%/yr
ASSERT-II: Detailed Inclusion Criteria

- Age ≥ 65
- and
  - $\text{CHA}_2\text{DS}_2\text{-VASc} \geq 2$, OR
  - Obstructive sleep apnea, OR
  - BMI >30
- and
  - Left atrial volume $\geq 58\text{ml}$ or LA diameter $\geq 4.4\text{cm}$, OR
  - Serum NT-ProBNP $\geq 290\ \text{pg/mL}$
ASSERT-II: Incidence of SCAF

Rate per year (95% CI)

- SCAF ≥ 5mins: 34.4% (27.7% – 42.3%)
- SCAF ≥ 30mins: 21.8% (16.7% – 27.8%)
- SCAF ≥ 6hours: 7.1% (4.5% – 10.6%)
- SCAF ≥ 24hours: 2.7% (1.2% – 5.0%)
Is SCAF common in non-PM patients?

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Device</th>
<th>Inclusion</th>
<th>Rate of AF Detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASSERT-II</td>
<td>250</td>
<td>SJM Confirm</td>
<td>Age&gt;65, AND CHADS-VASc≥2, or OSA, or BMI&gt; 30; AND LA&gt; 58mL, or NT-ProBNP &gt; 290 pg/mL</td>
<td>≥ 5 min 34.4% at one year</td>
</tr>
<tr>
<td>GRAF</td>
<td>200</td>
<td>MDT REVEAL-XT</td>
<td>Age ≥ 18 CHADS-VASc≥4</td>
<td>Pending</td>
</tr>
<tr>
<td>REVEAL-AF</td>
<td>450</td>
<td>MDT REVEAL-XT</td>
<td>Age ≥ 18 CHADS≥3, or CKD/COPD/OSA/CAD</td>
<td>29.3% at 18 months</td>
</tr>
<tr>
<td>PREDATE-AF</td>
<td>245</td>
<td>REVEAL-LINQ</td>
<td>Age&gt;18, AND CHADS-VASc≥2</td>
<td>≥ 6 min 22.4% at 451 days</td>
</tr>
<tr>
<td>DANISH LOOP</td>
<td>6000</td>
<td>REVEAL-LINQ (1500)</td>
<td>Age &gt; 70 One of HTN, DM, HF or stroke</td>
<td>Pending</td>
</tr>
</tbody>
</table>
Conclusions

- Unrecognized AF appears very common
  - Particularly in the elderly and those with AF/stroke risk factors

- Population-based AF screening may prevent stroke
  - Depends on implementation, acceptance, economics
  - Different populations, tools and strategies being tested

- Empiric therapy of patients at risk of AF and stroke under evaluation