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Should we perform mass screening for AF ?

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Screening for AF

- Who should we screen?
- How should we perform screening?

Wilson criteria for screening

- Condition should be an important health problem
- Natural history of the condition should be understood
- There should be a recognisable latent or early symptomatic stage
- There should be a test easy to perform and interpret, acceptable, accurate, reliable, sensitive and specific
- There should be an acceptable treatment
- Policy on who should be treated
- Diagnosis and treatment cost-effective
- Case-finding should be a continuous process

AF: Frequent Health problem

- Lifetime risk of developing AF in patients > 40y is 1 in 4
 - *Lloyd-Jones et al, Circulation 2004*
 - *From the Framingham Heart Study*
- Up to 75% of people do not experience symptoms while in AF
 - *Israel et al, JACC 2004*

Stroke: Important health problem

- 20% of CVAs are attributable to atrial fibrillation
- During AF, anticoagulation diminishes the risk of embolisms by 2/3
 - *Hart et al, Ann Intern Med 2007;146*
- 25% of CVAs are cryptogenic, or of undetermined source
 - *Hart et al, Lancet Neurol 2014;13*
- With AF, the annual rate of CVAs is 4.5%
 - *Arch Intern Med, 1994; 154: 1449-57*

Prevalence of silent AF

- Depends on the screened population
 - Age
 - Comorbidity
 - Recipient of pacemaker or defibrillator
 - Recent CVA or TIA
 - History of arrhythmia
- However depends mostly on duration of monitoring

SEARCH-AF

- 1000 patients, age > 65y
- Pharmacy screening
- iECG
 - AliveCor Kardia
- Newly identified AF in 1.5%

Opportunistic screening

- Screened subjects
 - Outpatient clinic – WatchBP and AliveCor
 - ≥ 65 years with diabetes or HTN
 - 1.17% incidence of AF
 - Increases with age (0.1% < 65 years, 0.9% 65-74, 3% ≥ 75 years)
Chan et al, Circulation 2016
- 65 years and more
 - Systematic review – 30 studies
 - 1.4%, number needed to screen 70
Lowres et al, Thromb Haemost 2013

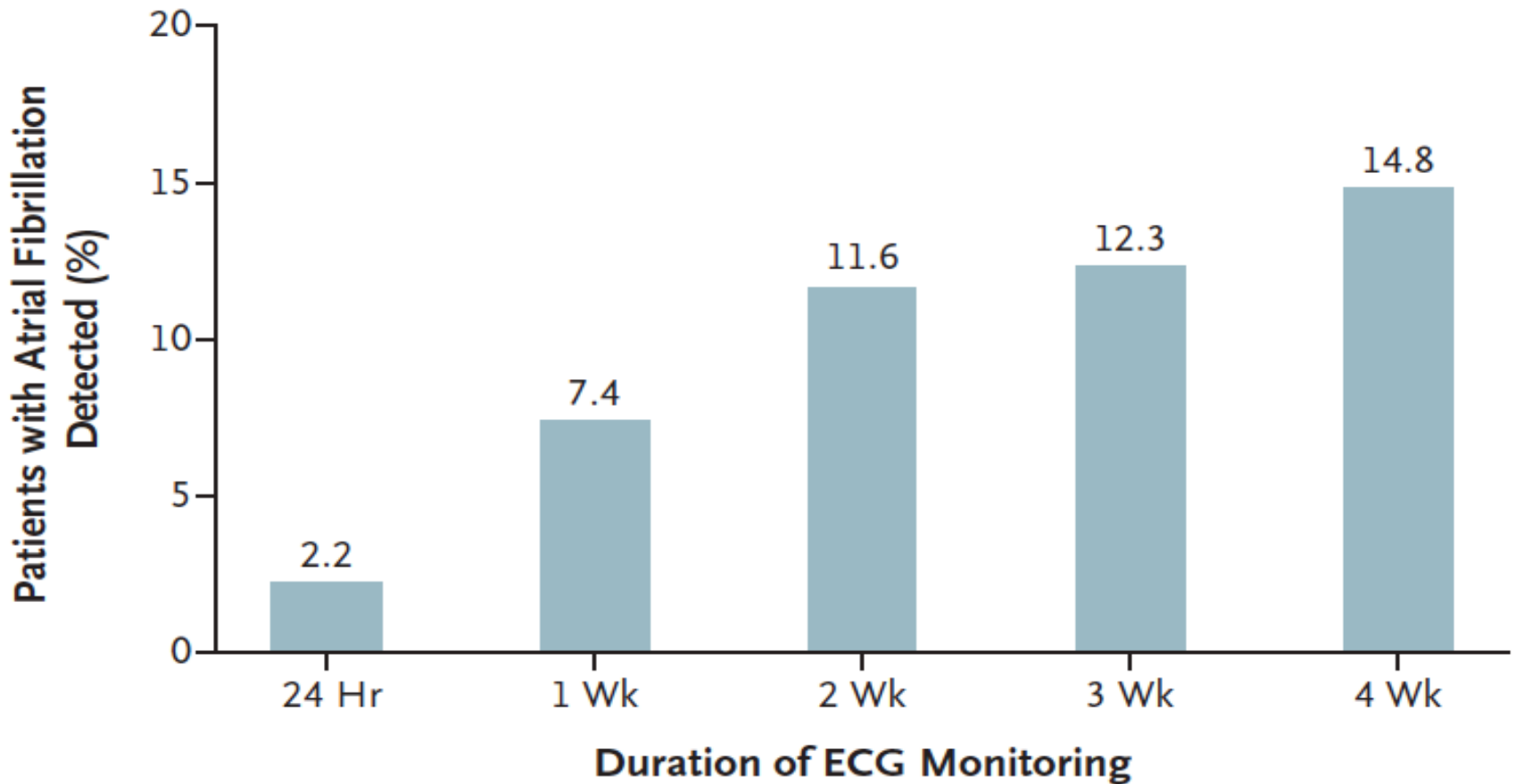
STROKESTOP Study

- Population screening in patients without known AF
- Individuals born in 1936-1937 (75 and 76 y at the time of the study) in Sweden
- 13 331 invitation to participate, 53.8% accepted
- Index ECG, twice daily ECG with handheld ECG recorder for 2 weeks
- New AF detected in 3.0% of patients
- 0.5% of newly diagnosed AF was found on index ECG

Subclinical AF

- 65 years and more
 - With elevated NT proBNP or LAE and CHADSVASc ≥ 2 or sleep apnea or BMI ≥ 30
 - 256 patients
 - Continuous subcutaneous monitoring
 - Mean follow up 16 ± 4 months
 - AF detection rate 34.4% (duration five minutes or more)

Long-term monitoring



Compliance: 82% of subjects completed > 3 weeks of monitoring

Population of patients with cryptogenic stroke

Anticoagulation begun in 18.6% of patients in the experimental group vs 11.1% in the control group

Embrace, NEJM, 2014

Prevalence of silent AF: Patients with Pacemaker or Defibrillator

TABLE 1 Incidence of newly detected AF in the population with implanted PPMs or ICDs

| Year | Trial | Device Indication | Clinical Profile of Patients | Incidence of AF |
|------|--------------------------------------|-----------------------------------|--|------------------|
| 2002 | Gillis et al ³⁷ | PPMs for SND | All | 157/231 (68%) |
| 2003 | MOST ³⁸ | PPMs for SND | All | 156/312 (50%) |
| 2010 | TRENDS ²¹ | PPMs and ICDs for all indications | History of prior stroke, no history of AF, no OAC use, ≥ 1 stroke risk factor | 45/163 (28%) |
| 2012 | TRENDS ³⁹ | PPMs and ICDs for all indications | History of prior stroke, no history of AF, no OAC use, ≥ 1 stroke risk factor | 416/1368 (30%) |
| 2012 | ASSERT ⁴⁰ | PPMs and ICDs for all indications | History of hypertension, no history of AF, no OAC use | 895/2580 (34.7%) |
| 2013 | Healey et al ⁴¹ | PPMs all indications | All | 246/445 (55.3%) |
| 2014 | Gonzalez et al ⁴² | PPMs all indications | No history of AF | 39/224 (17.4%) |
| 2015 | Benezet-Mazuecos et al ⁴³ | PPMs and ICDs for all indications | All | 28/109 (25.7%) |
| 2015 | Lima et al ⁴⁴ | PPMs all indications | No history of AF | 63/300 (21%) |
| 2016 | Benezet-Mazuecos et al ⁴⁵ | PPMs and ICDs for all indications | History of hypertension | 46/123 (37.3%) |

Abbreviations: AF, atrial fibrillation; ASSERT, Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial; ICDs, implantable cardioverter-defibrillators; MOST, Mode Selection Trial; OAC, oral anticoagulants; PPMs, permanent pacemakers; SND, sinus node disease TRENDS, The Relationship Between Daily Atrial Tachyarrhythmia Burden From Implantable Device Diagnostics and Stroke.

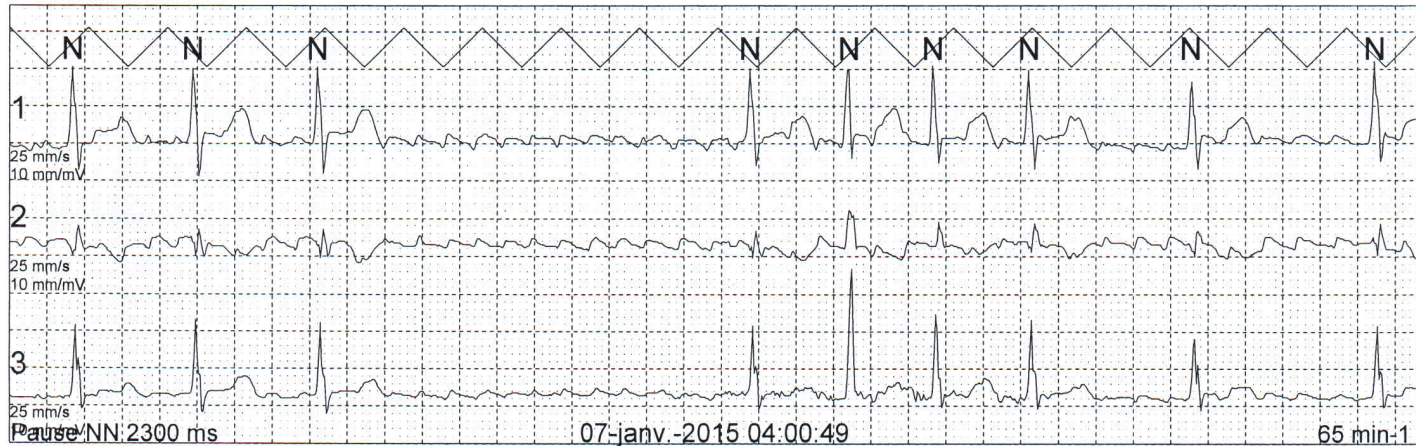
Consequences of silent AF

- One study 5550 patients with asymptomatic AF
- Adjusted stroke rate in 1460 untreated patients: 4% compared to 1% in matched control without AF
- Stroke risk in treated vs untreated patients: 1% vs 4%

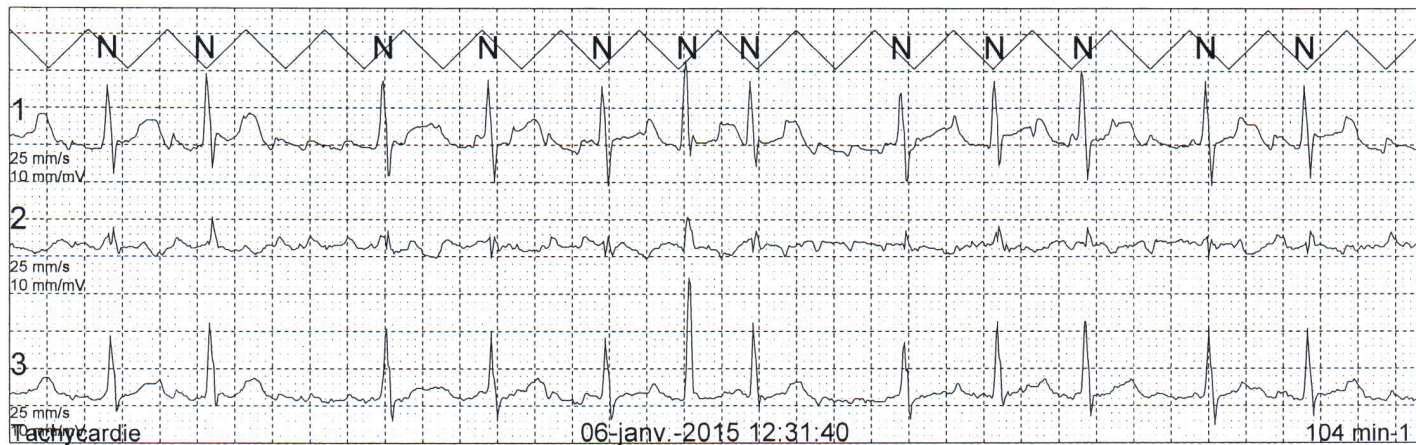
SCREENING / MONITORING DEVICES

Holter

RR max



RR min



Recording duration 24 hrs/48 hrs/7 days depending on model

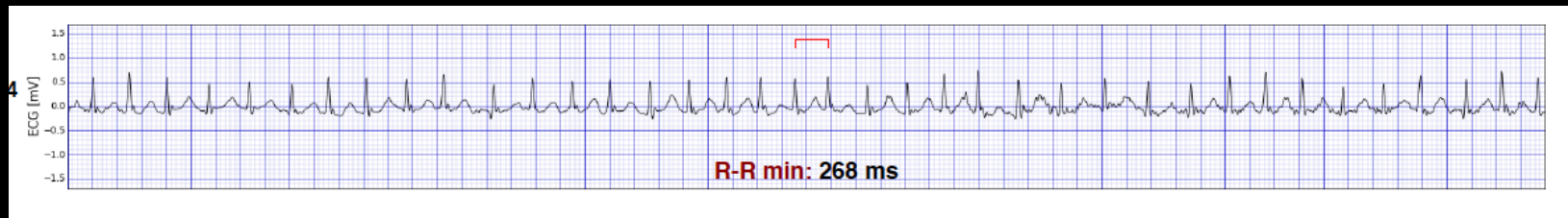
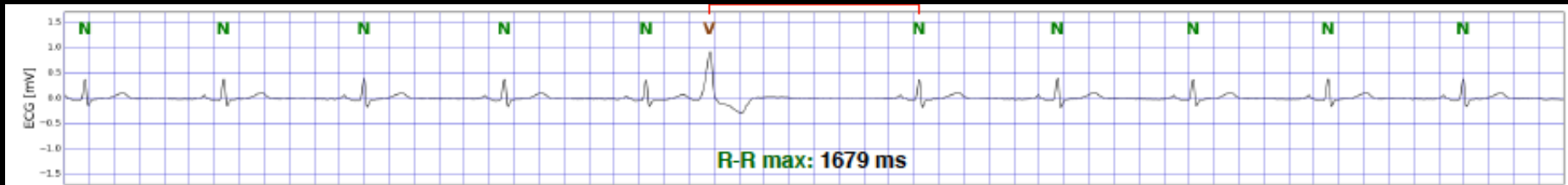
Cardiostat - Icentia



Continuous recording
duration up to 14 days

1 lead

Shower resistant
Replaceable electrodes



Zio patch - iRhythm



Continuous monitoring

Duration of monitoring up to 14 days

Repositioning not recommended

Not available in Canada

SEEQ - Medtronic



Continuous telemetry system

Data transmitted to Medtronic analysis centre

Analysis/notification 24/7

Monitoring duration up to 30 days

Not available clinically in Canada



SEEQ Wearable Sensor

Easy to apply, slim-profile sensor worn discreetly under shirt or blouse.



SEEQ Transmitter

Transmits data to Medtronic Monitoring Center

Spider Flash



External Loop Recorder (ELR)
Event recorder

Records up to 40 days (lithium battery)
or 15 days (alkaline battery)
Up to 25 hours of ECG 2 leads

Other companies have similar products
(King of Hearts, Braemar)

Analysis by medical electrophysiology
technician may take a lot of time

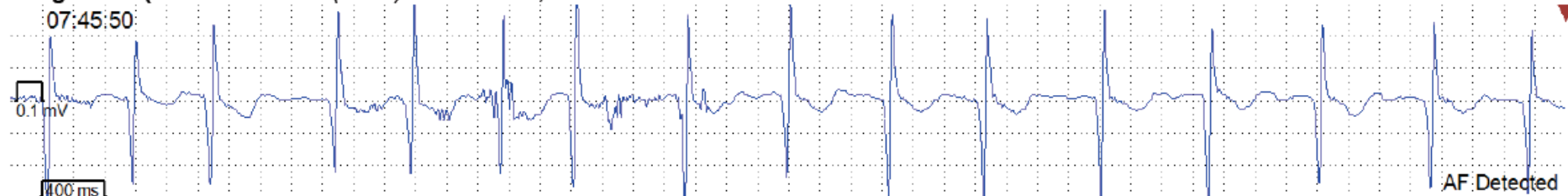
Internal Loop Recorder



Event monitor

Battery life: up to 3 years

Longest AF (last 14 months): (ID# 2) 26-Jun-2017, Duration: 02:12:00



Alive Cor Kardia

SEARCH-AF study

1000 patients

Pharmacy screening

New AF diagnosis in 1.5%

Automatic AF detection algorithm

Sensitivity 98.5%

Specificity 91.4%

Approved by FDA and Health Canada



iPhone

80 patients: 40 sinus rhythm, 40 AF
Compared to ECG

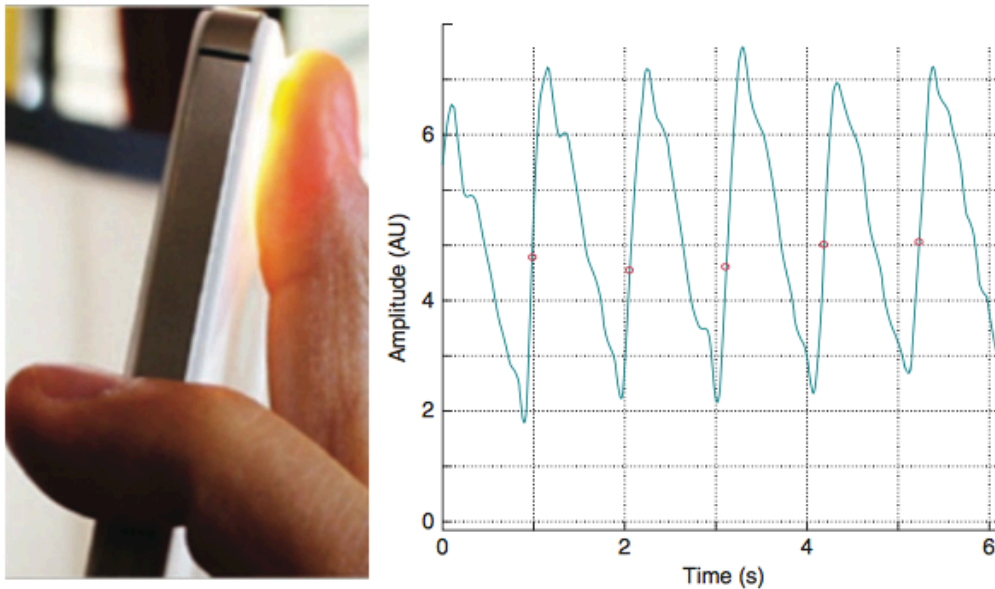
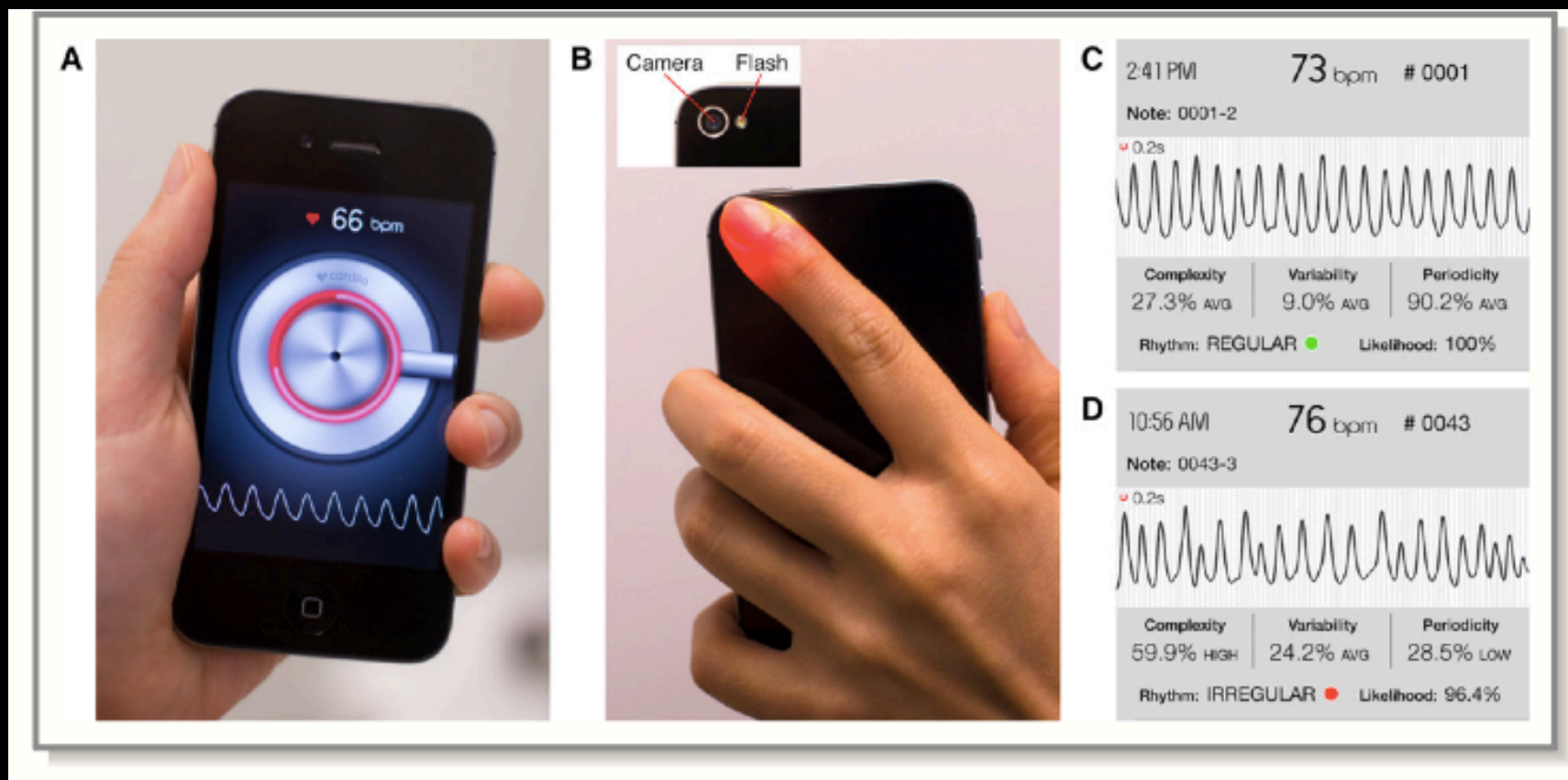


Figure 1 iPhone on index finger tip with resulting pulse wave signal of a patient with AF.

Filter and recording 2 minutes: Sensitivity 87.5% and specificity 95%

Filter and recording 5 minutes: Sensitivity 95% and specificity 95%

Cardio Rhythm



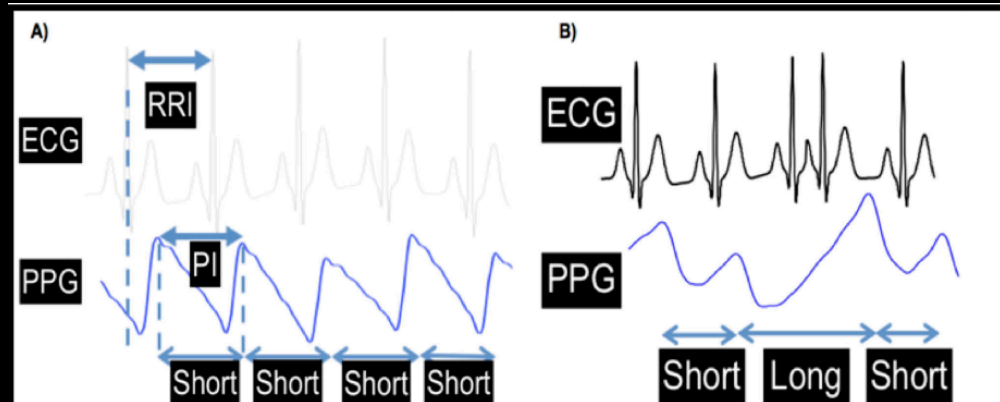
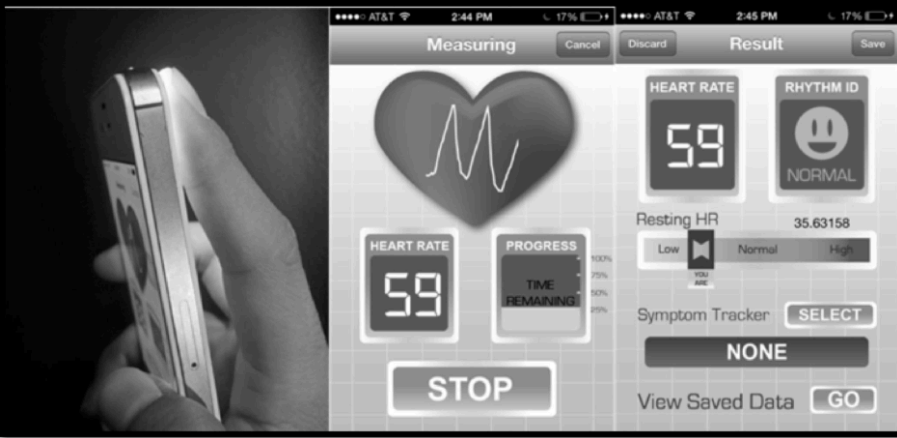
AF diagnostic based on absence of repeat pattern

Cardio Rhythm sensitivity 93%, specificity 98%, PPV 53%, NPV 99%

AliveCor sensitivity 71%, specificity 99%, PPV 77%, NPV 99%

Chan et al, Circulation 2016

PULSE-SMART



Pre- and post CVE
Two-minute recording
Compared to telemetry

| Algorithm | Sensitivity | Specificity | Accuracy |
|-----------------------------------|-------------|-------------|----------|
| Atrial Fibrillation | 0.970 | 0.935 | 0.951 |
| Premature atrial Contraction | 0.667 | 0.980 | 0.955 |
| Premature ventricular contraction | 0.733 | 0.976 | 0.960 |

AliveCor vs WatchBP Office AFIB

A

AliveCor Automated AF
Detector diagnosed AF

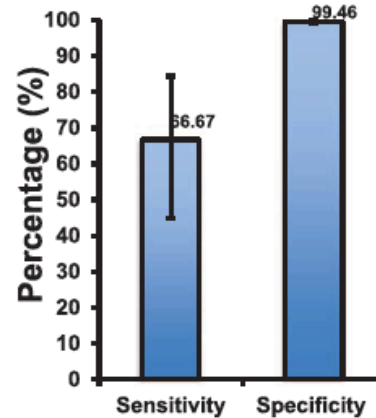
| True AF | |
|---------|-------|
| Yes | No |
| 16 | 11 |
| 8 | 2,017 |

Rhythm of 11 false positives

- 2 Sinus rhythm
- 6 PAC
- 3 Sinus arrhythmia

Rhythm of 2,017 true negatives

- 1870 Sinus rhythm
- 62 PAC
- 52 PVC
- 33 Sinus arrhythmia



B

MicroLife Afib
diagnosed AF

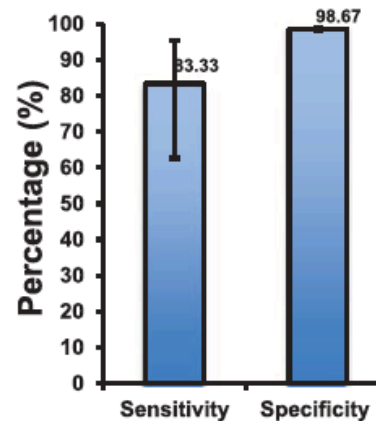
| True AF | |
|---------|-------|
| Yes | No |
| 20 | 27 |
| 4 | 2,001 |

Rhythm of 27 false positives

- 9 Sinus rhythm
- 11 PAC
- 1 PVC
- 6 Sinus arrhythmia

Rhythm of 2,001 true negatives

- 1863 Sinus rhythm
- 57 PAC
- 51 PVC
- 30 Sinus arrhythmia



*Photo not indicative, device tested Watch BP Office and not Watch BP Home

| Device | Method of Interpretation | Sensitivity (%) | Specificity (%) | Reference |
|----------------------------------|--|------------------|------------------|------------------------------|
| Pulse palpation | | 94 (84–97) | 72 (69–75) | Cooke et al ⁵⁵ |
| Handheld single-lead ECGs | | | | |
| AliveCor (Kardia) heart monitor | Algorithm only (based on presence of P wave and RR irregularity) | 98 (89–100) | 97 (93–99) | Lau et al ⁵⁶ |
| Merlin ECG event recorder | Cardiologist interpretation | 93.9 | 90.1 | Kearley et al ⁵⁷ |
| Mydiagnostick | Algorithm only (based on RR irregularity) | 94 (87–98) | 93 (85–97) | Tieleman et al ⁵⁸ |
| | | | | Vaes et al ⁵⁹ |
| Omron HCG-801 | Algorithm only (based on RR irregularity) | 98.7 (93.2–100) | 76.2(73.3–78.9) | Kearley et al ⁵⁷ |
| Omron HCG-801 | Cardiologist interpretation | 94.4 | 94.6 | Kearley et al ⁵⁷ |
| Zenikor EKG | Cardiologist interpretation | 96 | 92 | Doliwa et al ⁶⁰ |
| Modified blood pressure monitors | | | | |
| Microlife BPA 200 Plus | Algorithm only (based on pulse irregularity) | 92 | 97 | Marazzi et al ⁶¹ |
| Microlife BPA 200 | Algorithm only (based on pulse irregularity) | 97 (81.4–100) | 90 (83.8–94.2) | Wiesel et al ⁶² |
| Omron M6 | Algorithm only (based on pulse irregularity) | 100 | 94 | Marazzi et al ⁶¹ |
| Omron M6 comfort | Algorithm only (based on pulse irregularity) | 30 (15.4–49.1) | 97 (92.5–99.2) | Wiesel et al ⁶² |
| Microlife WatchBP | Algorithm only (based on pulse irregularity) | 94.9 (87.5–98.6) | 89.7 (87.5–91.6) | Kearley et al ⁵⁷ |
| Plethysmographs | | | | |
| Finger probe | Algorithm only (based on pulse irregularity) | 100 | 91.9 | Lewis et al ⁶³ |
| iPhone photo-plethysmograph | Algorithm only (based on pulse irregularity) | 97.0 | 93.5 | McManus et al ^{64*} |

New technologies

- The tech market is extremely invested in health and a great many of the tools that have come available are the subject of medical studies
- We can expect other technologies soon
 - Watches
 - Bracelets
 - Smart clothing
- Positive screening require ECG confirmation

Smartphones

- 64% of adults have a smartphone
- 50-64 years: 54%
- > 65 years: >27%

Should we screen for AF?

- AF is often asymptomatic or presents with atypical symptoms
- There is a treatment proven to reduce morbidity
- There are cheap, non invasive, available and reliable means for screening
- So YES!

Cost Effectiveness

- Based on data from STROKESTOP study
- Case based scenario for 1000 patients (75-76Y)
- 263 less patients with undetected AF
- 8 fewer strokes
- 11 more life-years
- 12 more quality adjusted life year (QALY)
- 4313 € per QALY
- 6583 € per avoided stroke

ESC guidelines

| Recommendations | Class | Level |
|---|------------|----------|
| Opportunistic screening for AF is recommended by pulse taking or ECG rhythm strip in patients >65 years of age. | I | B |
| In patients with TIA or ischaemic stroke, screening for AF is recommended by short-term ECG recording followed by continuous ECG monitoring for at least 72 hours. | I | B |
| It is recommended to interrogate pacemakers and ICDs on a regular basis for atrial high rate episodes (AHRE). Patients with AHRE should undergo further ECG monitoring to document AF before initiating AF therapy. | I | B |
| In stroke patients, additional ECG monitoring by long-term non-invasive ECG monitors or implanted loop recorders should be considered to document silent atrial fibrillation. | IIa | B |
| Systematic ECG screening may be considered to detect AF in patients aged >75 years, or those at high stroke risk. | IIb | B |

Arguments against screening

- There is increasing evidence that there is little temporal correlation between AF and stroke
- Although we know anticoagulation reduces stroke risk in patients with AF, we do not know if anticoagulation alters the risk of stroke in patients with short duration silent atrial arrhythmia (ongoing studies) – the duration threshold for anticoagulation is not yet clear

- Maybe the answer for now lies in the method of screening
- Long duration monitoring in patients without previous stroke in whom short duration AF is detected may bring more questions than answers
- Long duration monitoring for AF in patients with ESUS is required

- In patients without stroke:
- There is 86400 seconds in one day.
- Chances that a 30 seconds monitoring will catch a short duration non significant AF is quite small. More chances of missing paroxysmal AF than chances of catching non significant AF.

Screening

- Opportunistic screening in patients $\geq 65Y$ OR CHADS score ≥ 1 using a short duration rhythm strip/ECG/pulse taking
 - Handheld ECG seems the best approach – other means (pulse palpation, pulse oxymetry) need ECG confirmation
- Longer duration screening in high risk patients – after ESUS – next talk!
- Areas for consideration for longer duration although no recommendation
 - Sleep apnea, heart failure, large left atrium, high PAC burden

Final word

- Screening for AF should be performed
- Duration of recording should depend on underlying risk of stroke/AF
- There is an urgent need to better define treatment threshold for short AF episodes less than 24h in patients without prior stroke
- With technological progress, continuous monitoring with watches / bracelets will soon be available and the question whether the AF burden needed to initiate anticoagulation will extend beyond the pacemaker clinic