Disclosures

• I have no actual or potential conflict of interest in relation to this program/presentation

• I will not be discussing “off-label” uses of the any medications or devices

• I do own and wear a series 4 Apple Watch
Live Content Slide

When playing as a slideshow, this slide will display live content

Poll: Do you wear an Apple Watch?
The Apple Heart Study

• *Not yet published*
• Presented at the annual ACC Meeting at New Orleans, March 2019
• Sponsored by Apple, conducted by Stanford University w/ other US sites
• Principal Investigators : Mintu Turakhia MD MAS, Marco Perez MD
Background

• 700,000 people in the US may have previously unknown AF, w/ incremental cost burden of $3.2B
  • High CV morbidity

• Traditional methods to detect AF
  • Physical exam for irregular pulse, resting EKG, continuous 2-14 day monitor, episodic home based monitoring : not sensitive enough
  • Implantable monitors : expensive and inconvenient
• “Wearables” measure pulse rate from the wrist using photoplethysmography (PPG), using optical sensor
• Pulse data analyzed for *irregularity and variability*
• Requires “*gold-standard*” for confirmation
• Provision for clinical evaluation needed, otherwise potential for harm
Irregular Pulse Notification Algorithm

Tachogram = Periodic, opportunistic measurements
5 confirmations $\Rightarrow$ notify user

Positive triggers frequent measurements
Not confirmed $\Rightarrow$ return to usual sampling

The algorithm does not use the watch ECG feature
Overall Goals

To evaluate the ability of the irregular pulse notification algorithm to identify atrial fibrillation and guide subsequent evaluation

- Notification burden
- Subsequent Afib diagnosis
- Algorithm performance
- Safety
- Pragmatic and generalizable
- Scalable procedures
Prospective, Single Arm, Open Label Study

Overall Cohort
- Study App
- Notification
  - Irregular Rhythm Identified
- Connect to Telehealth Doctor
  - Board certified physicians available US-wide 24/7
- Mail ECG Patch
- Discuss Heart Results
  - Review results with telehealth doctor
- 90-Day / EOS Follow-Up
  - Insights into care pathway

Inclusion criteria
- Age ≥ 22; U.S. Resident
- iPhone (5S or higher) + Watch (Series 1-3)

Exclusion criteria
- Atrial fibrillation or atrial flutter
- Current use of anticoagulation
Primary Endpoints

Afib > 30 seconds on ECG patch in ≥ 65 years

Simultaneous Afib on ECG Patch and individual tachogram

Secondary Endpoints

Simultaneous Afib on ECG Patch w/ notification

Self-reported contact w/ health care provider

Irregular Rhythm Identified

Connect to Telehealth Doctor

Mail ECG Patch

Discuss Heart Results
Study Size

- Single arm study with enrollment goal of 500,000
- Assumption was to have 503 patches in age > 65 and < 65
- Cumulative enrollment: 419,297 subjects, 24,626 of age > 65
- Enrollment from Nov 2017 through July 2018
- Last data collection Feb 2019
Consort Diagram

- Total Population: 419,297
  - Pulse Notification: 2,161 (0.5%)
    - First Study Visit: 945 (44%)
      - At SV1: 291 (31%)
        - Emergent symptoms: 20
        - Prior Afib of flutter: 174
        - Current Anticoagulant use: 90
        - Other reasons: 33
      - ECG Patch Shipped: 658 (70%)
    - ECG Patch Returned & Analyzed: 450 (68%)
  - No Notification (PN): 417,136 (99.5%)
    - Completed 90-day Survey: 1,376 / 2,161 (64%)
    - Completed EOS Survey: 929 / 2,161 (43%)

450 / 2161 = 21%
## Demographics

<table>
<thead>
<tr>
<th></th>
<th>Overall Cohort</th>
<th>Notification</th>
<th>ECG Patch</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>419,297</td>
<td>2,161</td>
<td>450</td>
</tr>
<tr>
<td>Female (%)</td>
<td>177,087 (42)</td>
<td>461 (21)</td>
<td>102 (23)</td>
</tr>
<tr>
<td>Age, mean (sd)</td>
<td>41 (13)</td>
<td>57 (15)</td>
<td>59 (14)</td>
</tr>
<tr>
<td>≥ 65</td>
<td>24,626 (6)</td>
<td>775 (36)</td>
<td>181 (40)</td>
</tr>
<tr>
<td>55–64</td>
<td>42,633 (10)</td>
<td>556 (26)</td>
<td>114 (25)</td>
</tr>
<tr>
<td>40–54</td>
<td>132,696 (32)</td>
<td>488 (23)</td>
<td>106 (24)</td>
</tr>
<tr>
<td>22–39</td>
<td>219,179 (52)</td>
<td>341 (16)</td>
<td>49 (11)</td>
</tr>
<tr>
<td>White</td>
<td>286,190 (68)</td>
<td>1,747 (81)</td>
<td>379 (84)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>48,775 (12)</td>
<td>104 (5)</td>
<td>20 (4)</td>
</tr>
<tr>
<td>African American</td>
<td>32,275 (8)</td>
<td>106 (5)</td>
<td>16 (4)</td>
</tr>
<tr>
<td>Asian</td>
<td>26,156 (6)</td>
<td>87 (4)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Other Mixed Ethnicity</td>
<td>7,958 (2)</td>
<td>32 (1)</td>
<td>6 (1)</td>
</tr>
</tbody>
</table>
## Initial Irregular Pulse Pulse Notifications

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Notified / Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>2,161 / 419,297</td>
<td>0.52</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 65</td>
<td>775 / 24,626</td>
<td>3.2</td>
</tr>
<tr>
<td>55–64</td>
<td>556 / 42,633</td>
<td>1.3</td>
</tr>
<tr>
<td>40–54</td>
<td>488 / 132,696</td>
<td>0.37</td>
</tr>
<tr>
<td>22–39</td>
<td>341 / 219,179</td>
<td>0.16</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>461 / 177,087</td>
<td>0.26</td>
</tr>
<tr>
<td>Male</td>
<td>1,672 / 238,700</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Percent of subjects notified

Overall Cohort ~ 8 Months Monitoring
Atrial Fibrillation on *Subsequent* ECG Patch

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Observed AF / Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>153 / 450</td>
<td>34</td>
</tr>
<tr>
<td>≥ 65</td>
<td>63 / 181</td>
<td>35</td>
</tr>
<tr>
<td>55–64</td>
<td>47 / 114</td>
<td>41</td>
</tr>
<tr>
<td>40–54</td>
<td>34 / 106</td>
<td>32</td>
</tr>
<tr>
<td>22–39</td>
<td>9 / 49</td>
<td>18</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>26 / 102</td>
<td>26</td>
</tr>
<tr>
<td>Male</td>
<td>124 / 335</td>
<td>37</td>
</tr>
</tbody>
</table>

Mean time to hook up: 13 days
Mean wear time: 6.3 days
Positive Predictive Values

<table>
<thead>
<tr>
<th>Afib on ECG patch</th>
<th>Positive Tachograms</th>
<th>PPV (97.5% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall 1489</td>
<td>2089</td>
<td>0.71 (0.69-0.74)</td>
</tr>
<tr>
<td>Age &gt; 65 548</td>
<td>914</td>
<td>0.60 (0.56-0.64)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Afib on ECG patch</th>
<th>Positive Notifications</th>
<th>PPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall 72</td>
<td>86</td>
<td>0.84 (0.76-0.92)</td>
</tr>
<tr>
<td>Age &gt; 65 25</td>
<td>32</td>
<td>0.78 (0.64-0.92)</td>
</tr>
</tbody>
</table>
Burden of Atrial Fibrillation

- 24 hour: 25.5%
- 6 hour: 34%
- 1 hour: 29.4%
- 6 min: 5.9%
- 30 sec: 5.2%

Total: 89%
90 Day Survey

Notification

2161 (0.5%) → 1376/2161 (64%) → 787/1376 (57%)

90 Day Survey

161 (15%) Afib before enrollment

Contacted Non Study Provider

218 (28%) start new medication
262 (33%) referral to specialist
287 (37%) additional testing
Poll: In your opinion, what Positive Predictive Value is the minimal acceptable for a wearable for predicting atrial fibrillation?
Poll: Based on the results of the Apple Heart Trial, how likely are you to recommend a similarly functioning wearable to your slightly elevated risk, worried well patient?
Poll: Would the detection of PVCs and ST shifts (ischemia) on the ECG algorithm in addition to Afiib detection change your likelihood of "prescribing" a wearable and if so, by now much?
Conclusions

• Novel virtual design
• Low notification percent (0.5%)
• ECG patch 13 days after notification – 34% had Afib
• PPV – Tachogram: 0.71, Notification: 84%
• 57% of those notified contacted Non-study provider
• Exposure to App was safe
Limitations

• Higher than anticipated drop offs after notification
• Fewer ECG patches than planned
• Virtual Study Design (large, quick, pragmatic study)
  • Relied on self-assessment of enrollment criteria, outcomes