

Results of a Large-scale, App-based Study to Identify Atrial Fibrillation Using a Smartwatch: The Apple Heart Study



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on behalf of the Apple Heart Study Investigators

NCT # 03335800

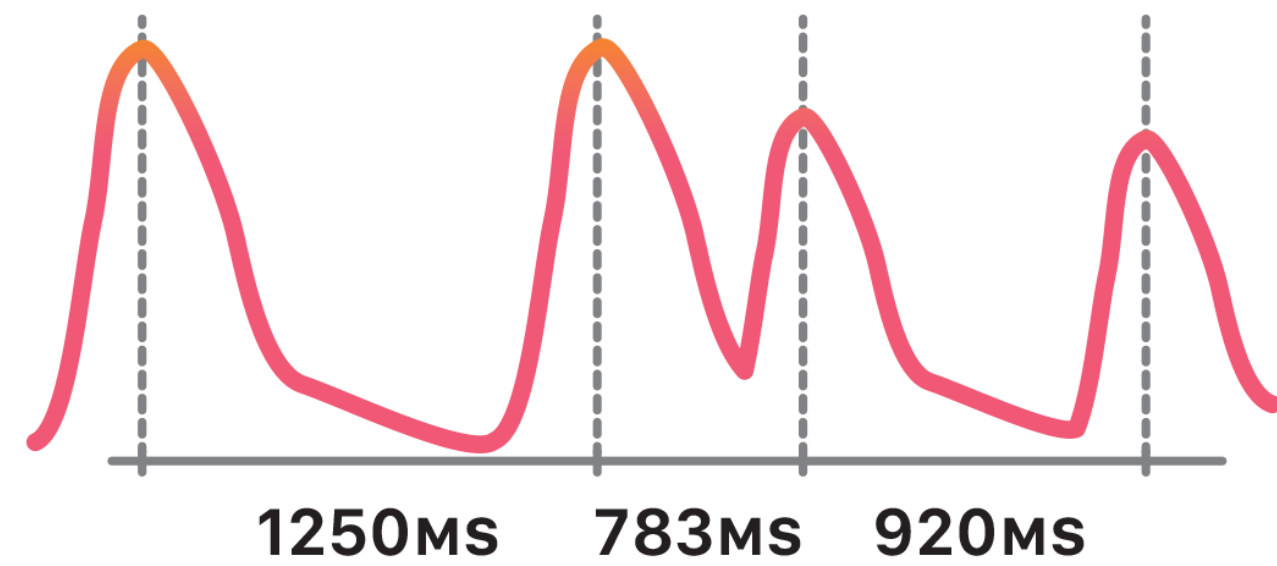


Introduction

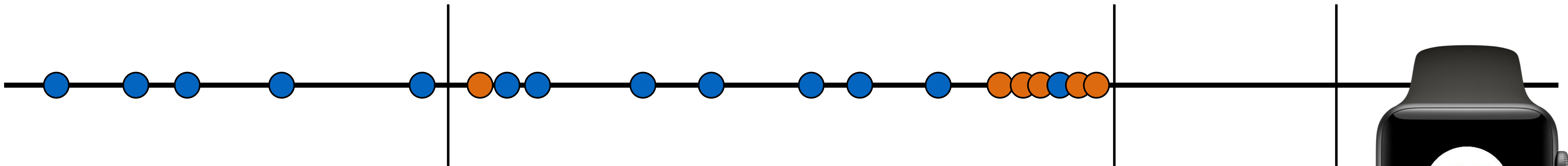
- Optical sensor detects pulse waveform to passively measure heart rate
- Detection of pulse irregularity may be useful to identify atrial fibrillation ("Afib")



Irregular Pulse Notification Algorithm



- Algorithm results
- Regular pulse
 - Suggestive of Afib



Tachogram = Periodic, opportunistic measurements

5 confirmations \Rightarrow notify user

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



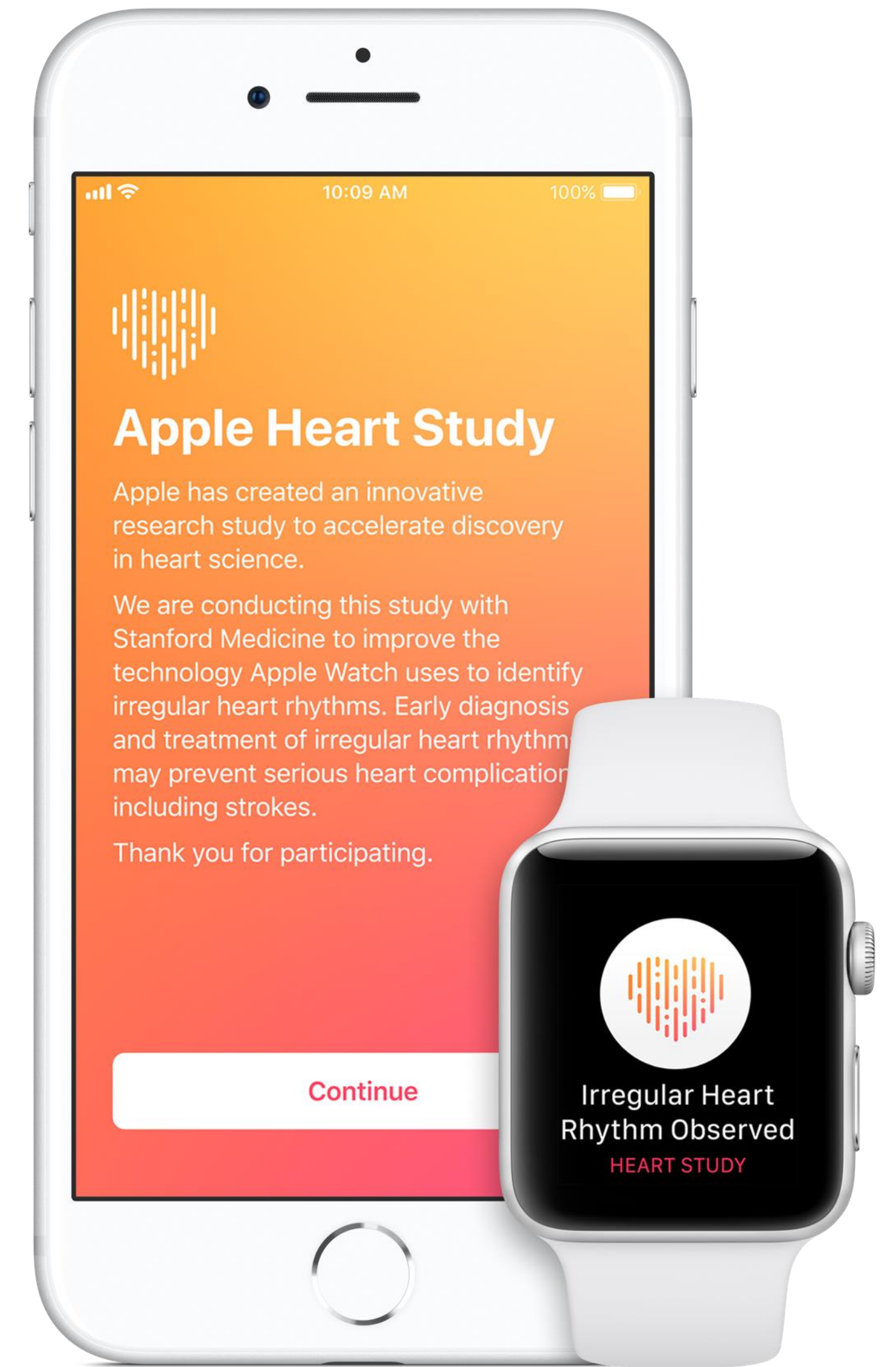
The algorithm does not use the watch ECG feature



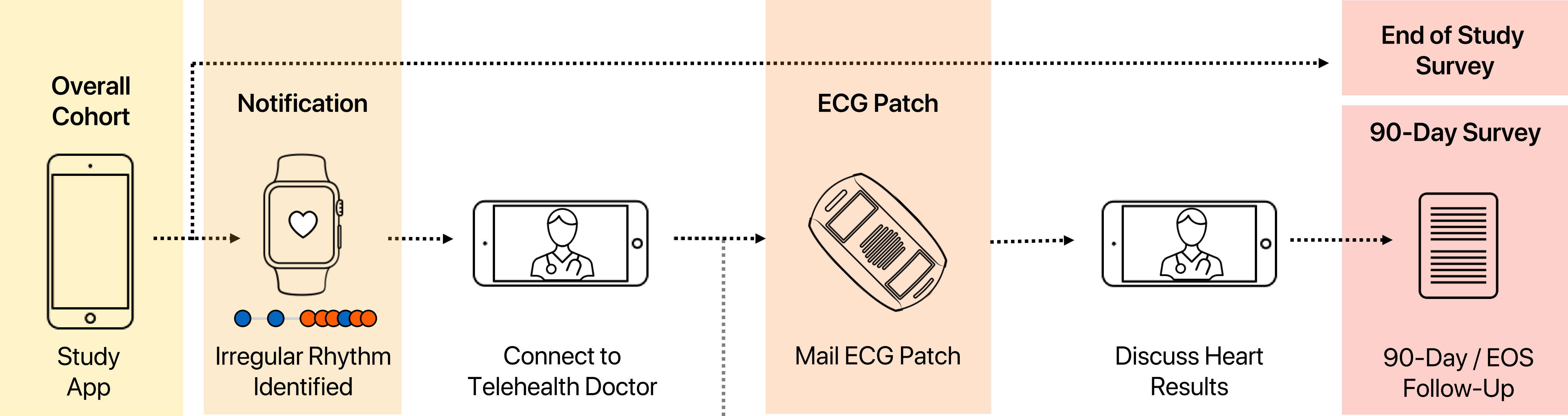
Overall Goal

To evaluate the ability of the irregular pulse notification algorithm to identify Afib and guide subsequent clinical evaluation

- Notification burden
- Subsequent Afib diagnosis
- Algorithm performance
- Safety
- Pragmatic and generalizable
- Scalable study procedures



Prospective, Single Arm, Open Label Study



Inclusion criteria

- Age \geq 22; U.S. Resident
- iPhone (5S or higher) + Watch (Series 1-3)

Exclusion criteria

- Atrial fibrillation or atrial flutter
- Current use of anticoagulation

American Well®

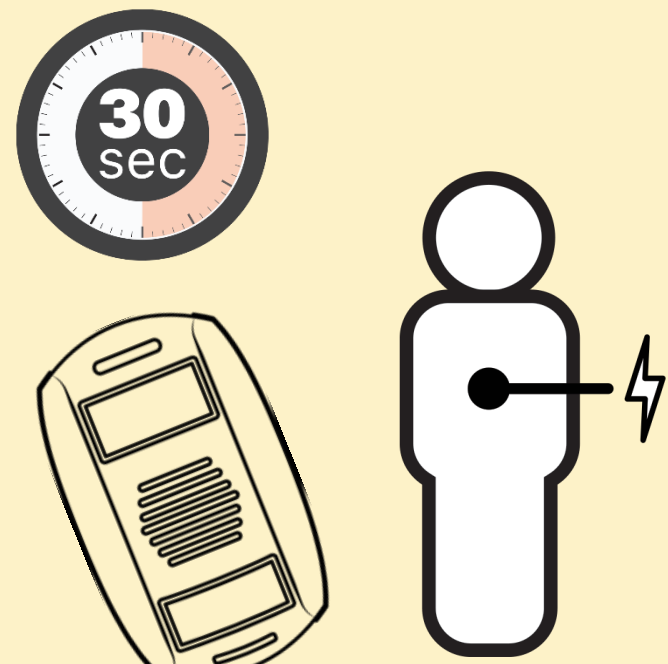
BioTelemetry inc.

Urgent or
Emergency Care

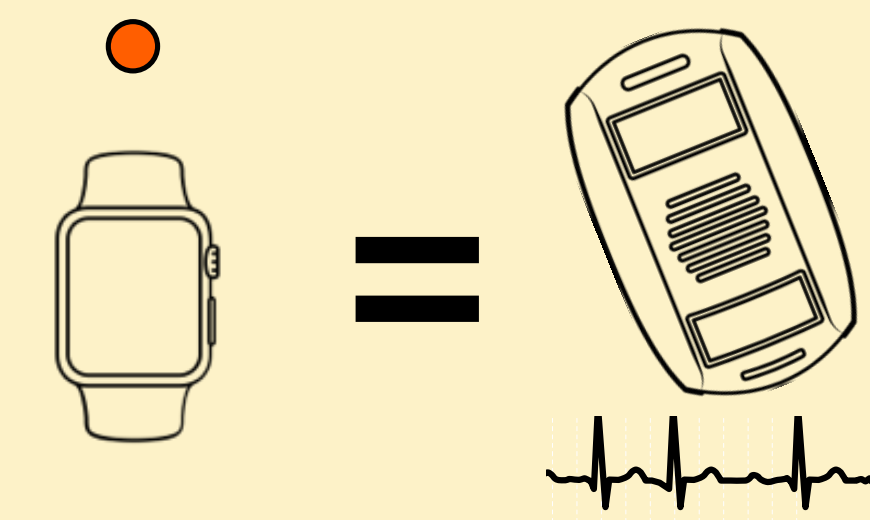


Primary Endpoints

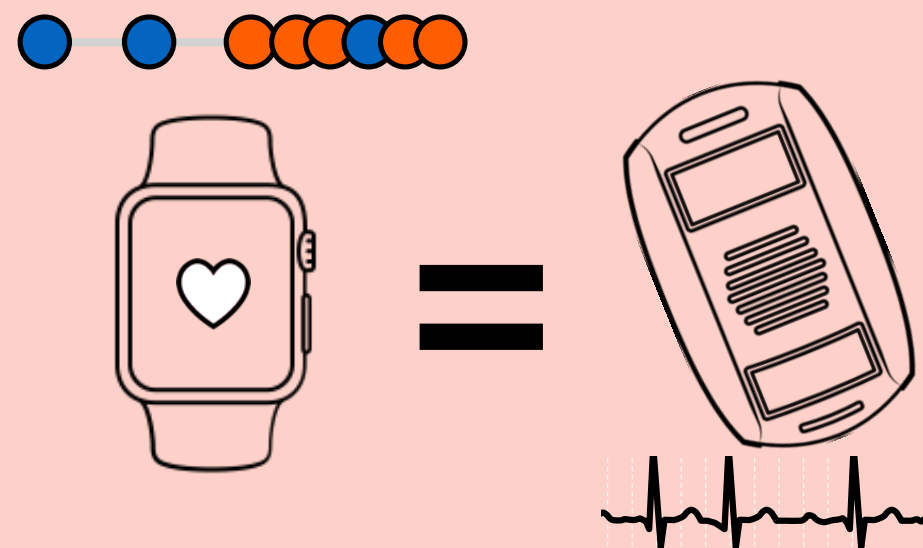
Secondary Endpoints



Afib > 30 seconds
on ECG patch
in ≥ 65 years



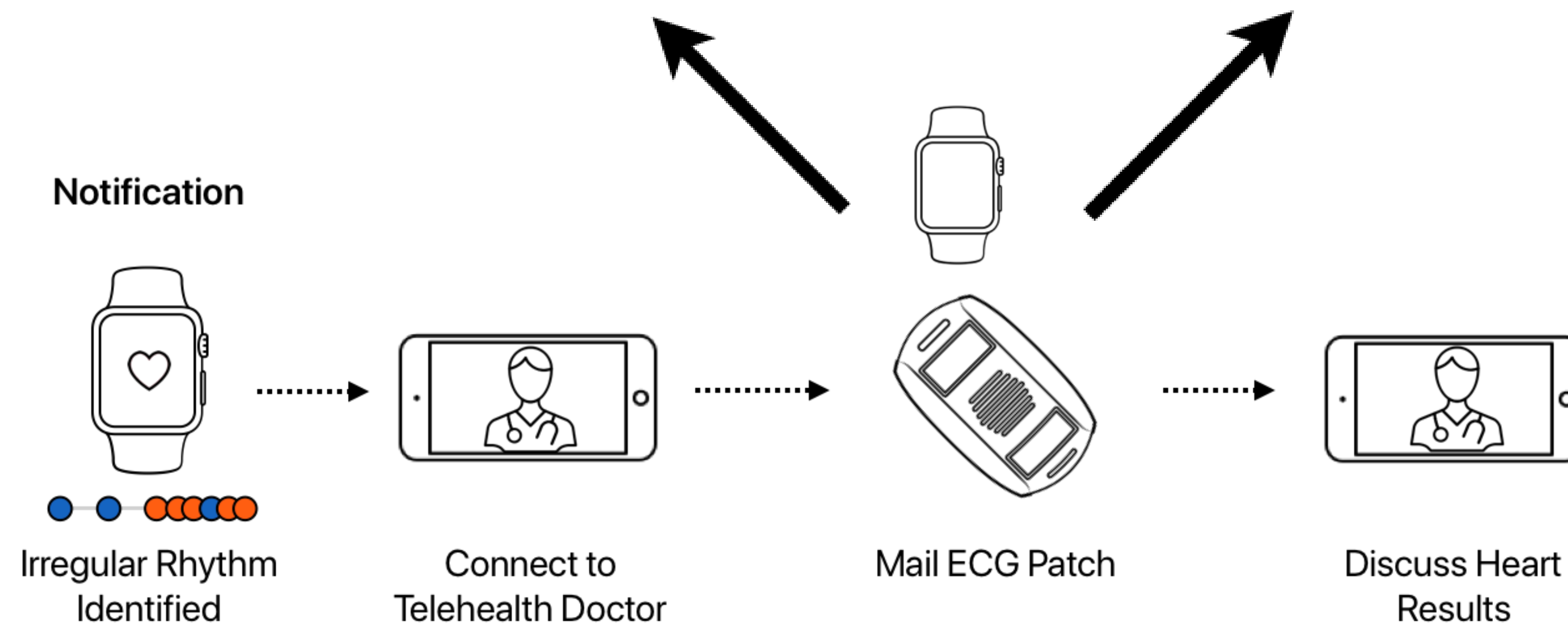
Simultaneous Afib on
ECG Patch and
individual tachogram



Simultaneous Afib on
ECG Patch w/ notification



Self-reported contact
w/ health care provider

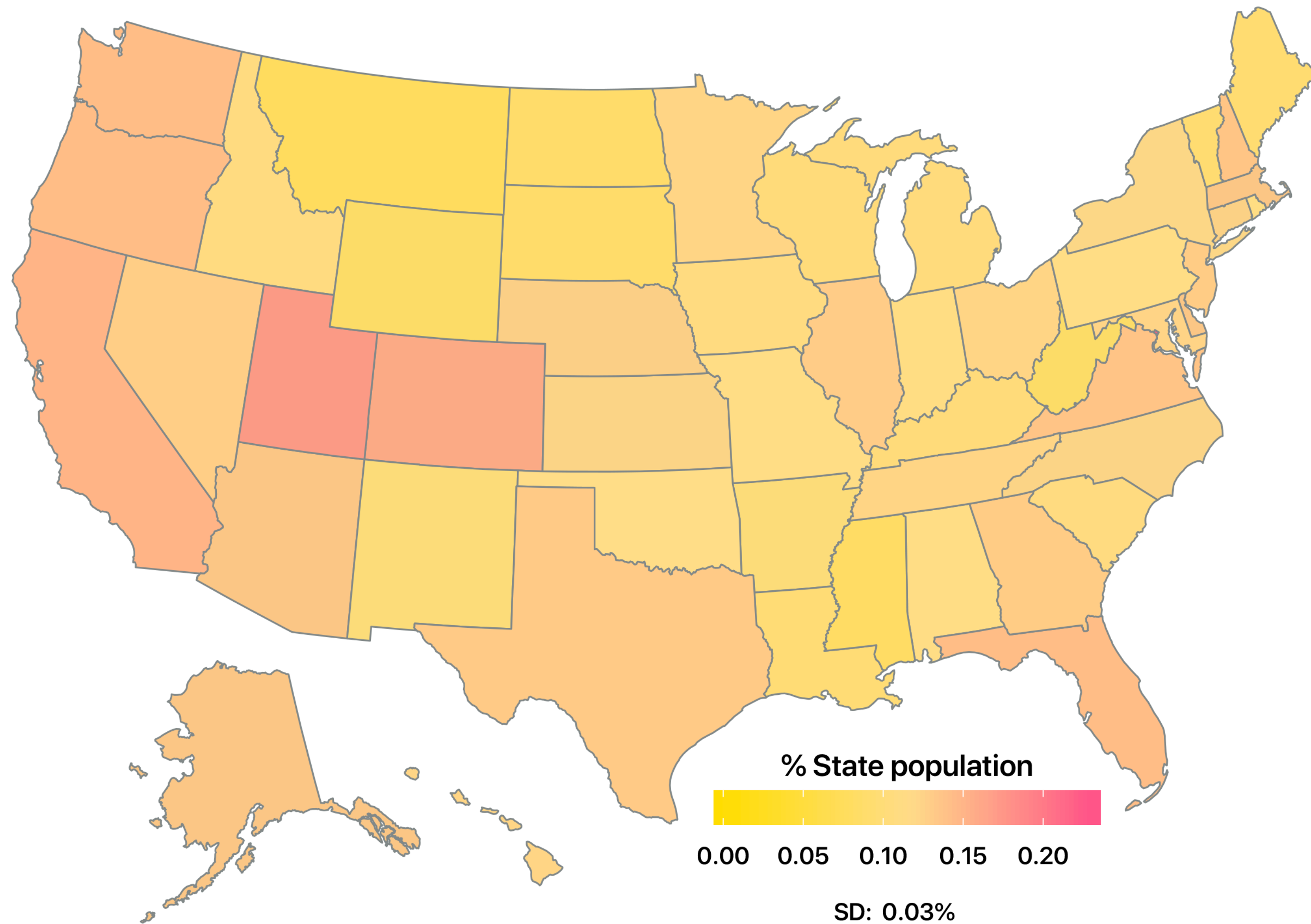


Statistical Considerations

- Single-arm study with an enrollment goal of up to 500,000
 - Assumption was to have 503 patches in age ≥ 65 and < 65
- Designed to have sufficient precision to estimate
 - The yield of **Afib on subsequent ECG patch** with 97.5% confidence intervals (CI) no wider than 10% in age ≥ 65 and overall
 - The positive predictive value or **PPV of an individual tachogram with simultaneous ECG patch** in age ≥ 65 and overall
 - 97.5% CI lower bound >0.70 and upper bound ≥ 0.75



Enrollment: 419,297; 24,626 age \geq 65

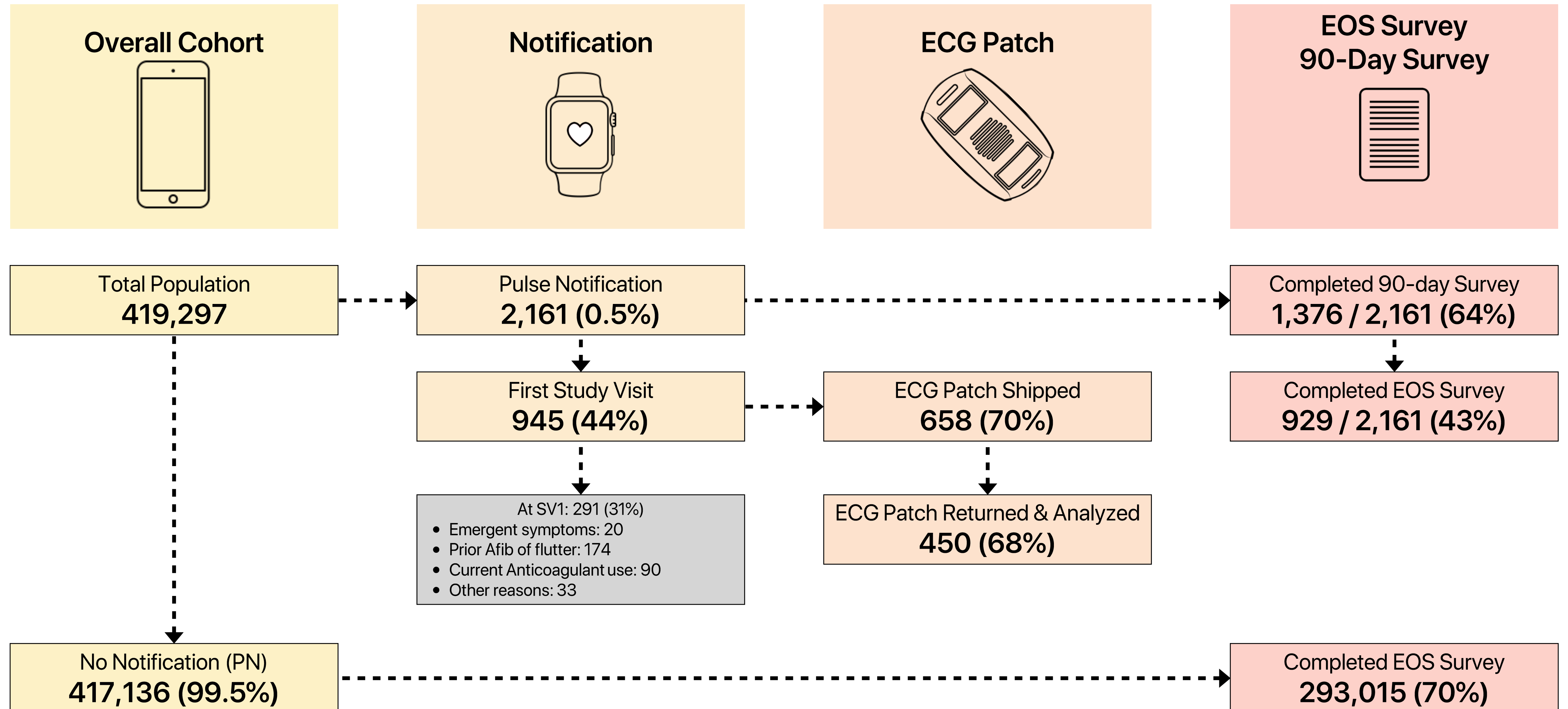


Enrollment:
Nov 29, 2017 – Jul 31, 2018

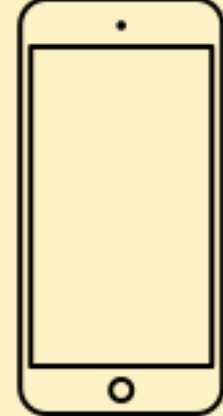

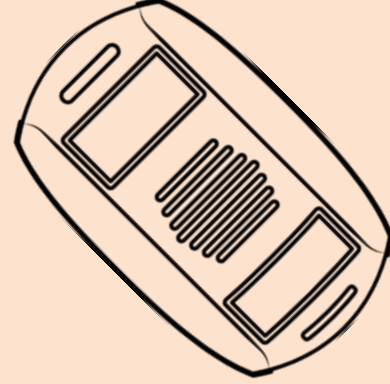
Last data collection:
Feb 25, 2019



Consort Diagram



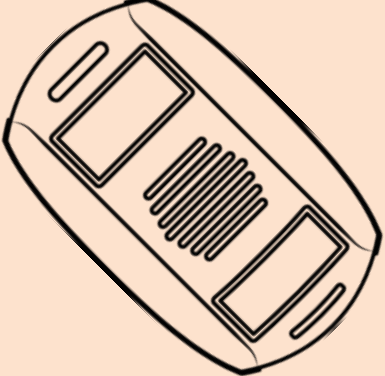


Baseline Demographics

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



Baseline Demographics *(continued)*

| | Overall Cohort  | Notification  | ECG Patch  |
|---|---|---|--|
| N | 419,297 | 2,161 | 450 |
| CHA ₂ DS ₂ VASc ≥ 2 | 55,277 (13) | 713 (33) | 171 (38) |
| Obesity (%) | 160,197 (38) | 984 (46) | 192 (43) |
| Hypertension (%) | 86,338 (21) | 917 (42) | 200 (44) |
| Diabetes (%) | 20,443 (5) | 255 (12) | 53 (12) |
| Heart failure (%) | 2,511 (0.6) | 72 (3) | 10 (2) |
| Stroke (%) | 4,153 (1) | 66 (3) | 10 (2) |
| Peripheral Arterial Disease (%) | 2,596 (0.6) | 52 (2) | 10 (2) |
| Smoking (any) | 25,458 (6) | 88 (4) | 10 (2) |
| Alcohol (≥ 1 drink/week) | 190,463 (45) | 1,092 (51) | 227 (50) |



Results

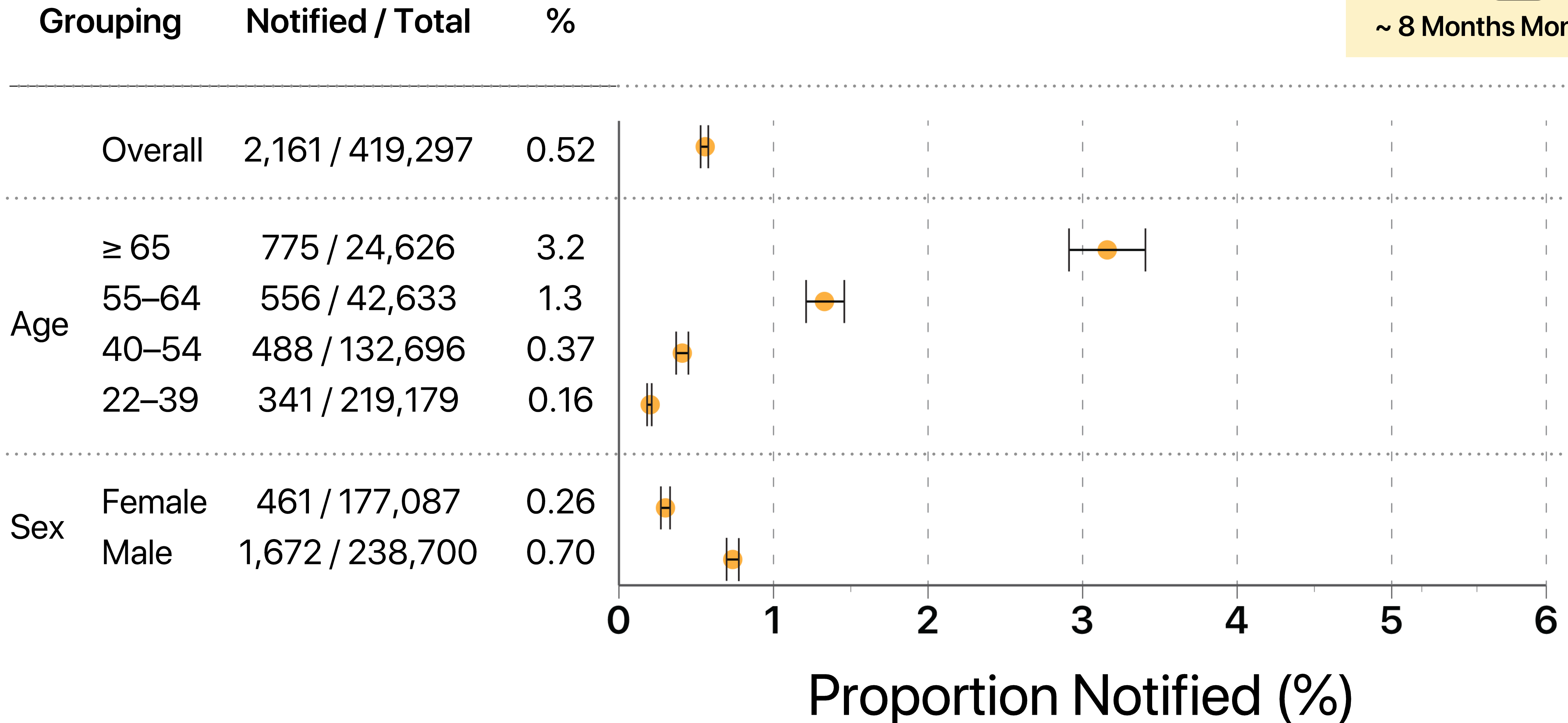


Initial Irregular Pulse Notifications

Overall Cohort

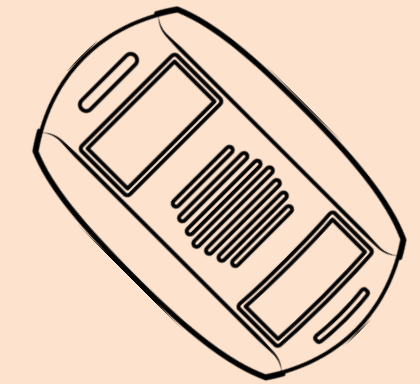


~ 8 Months Monitoring

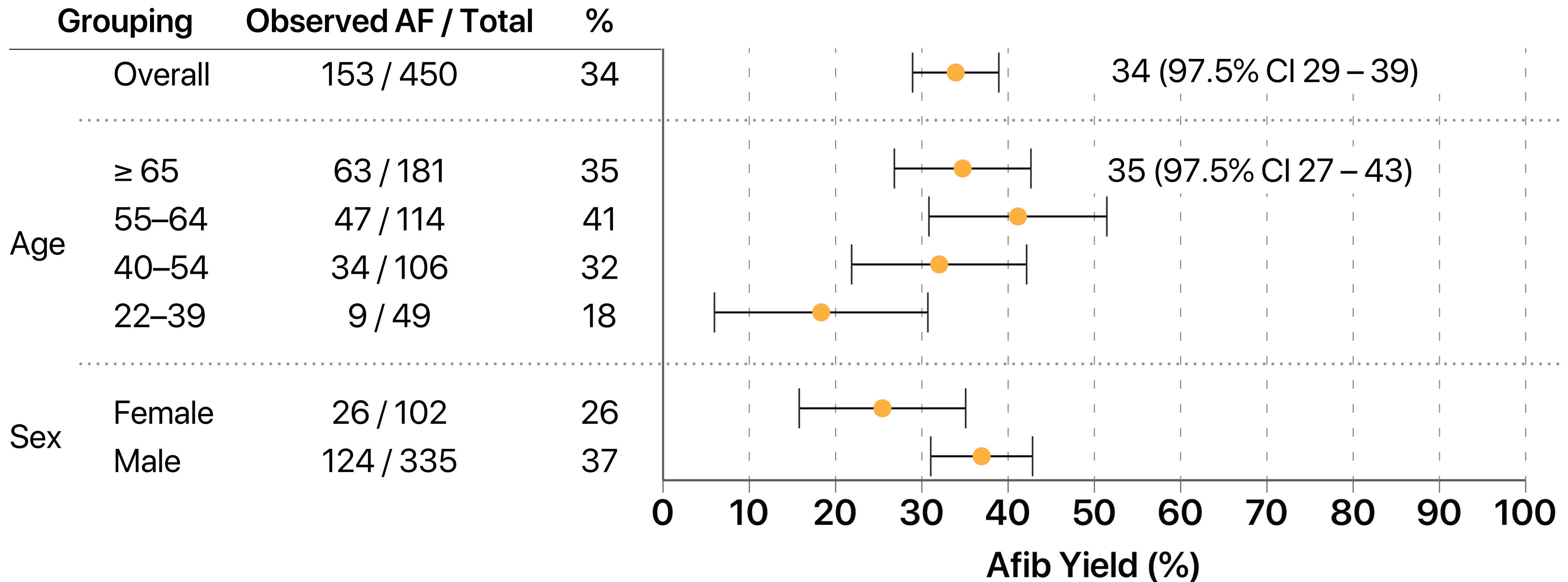


Afib Yield on ECG Patch

ECG Patch 450

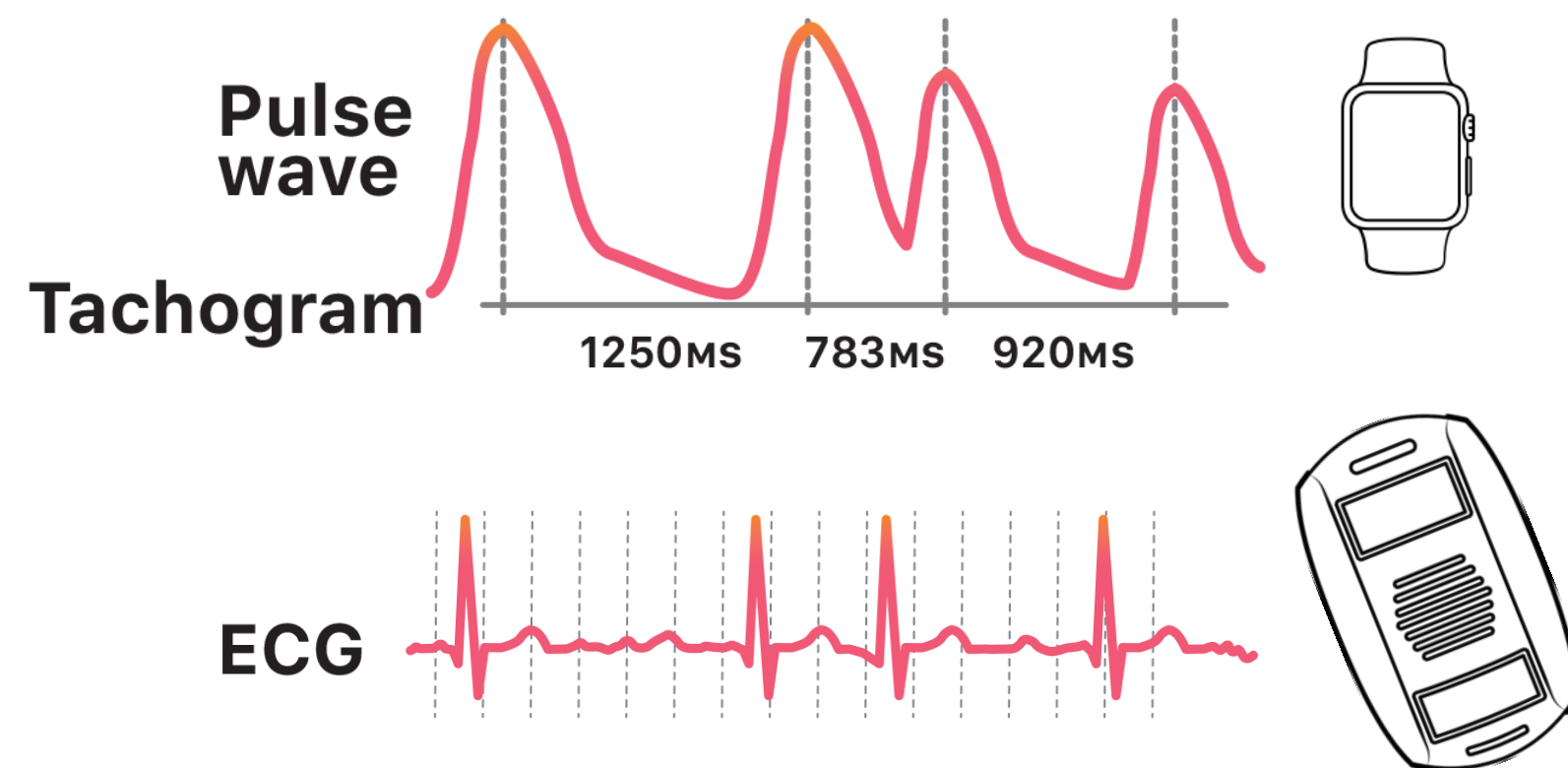


Mean time to hookup: 13 days
Mean wear time: 6.3 days

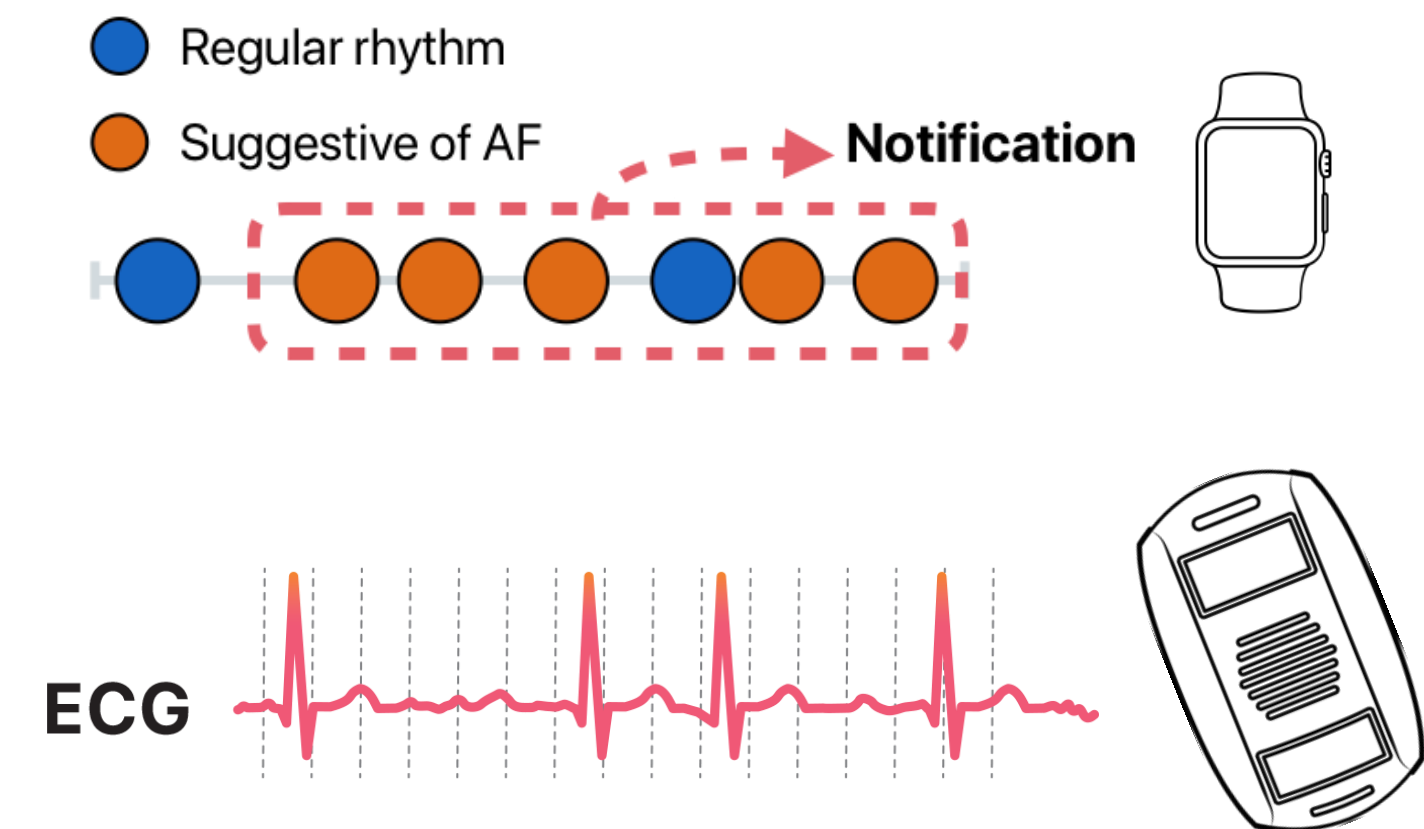


Positive Predictive Values

Irregular Tachograms



Irregular Pulse Notifications



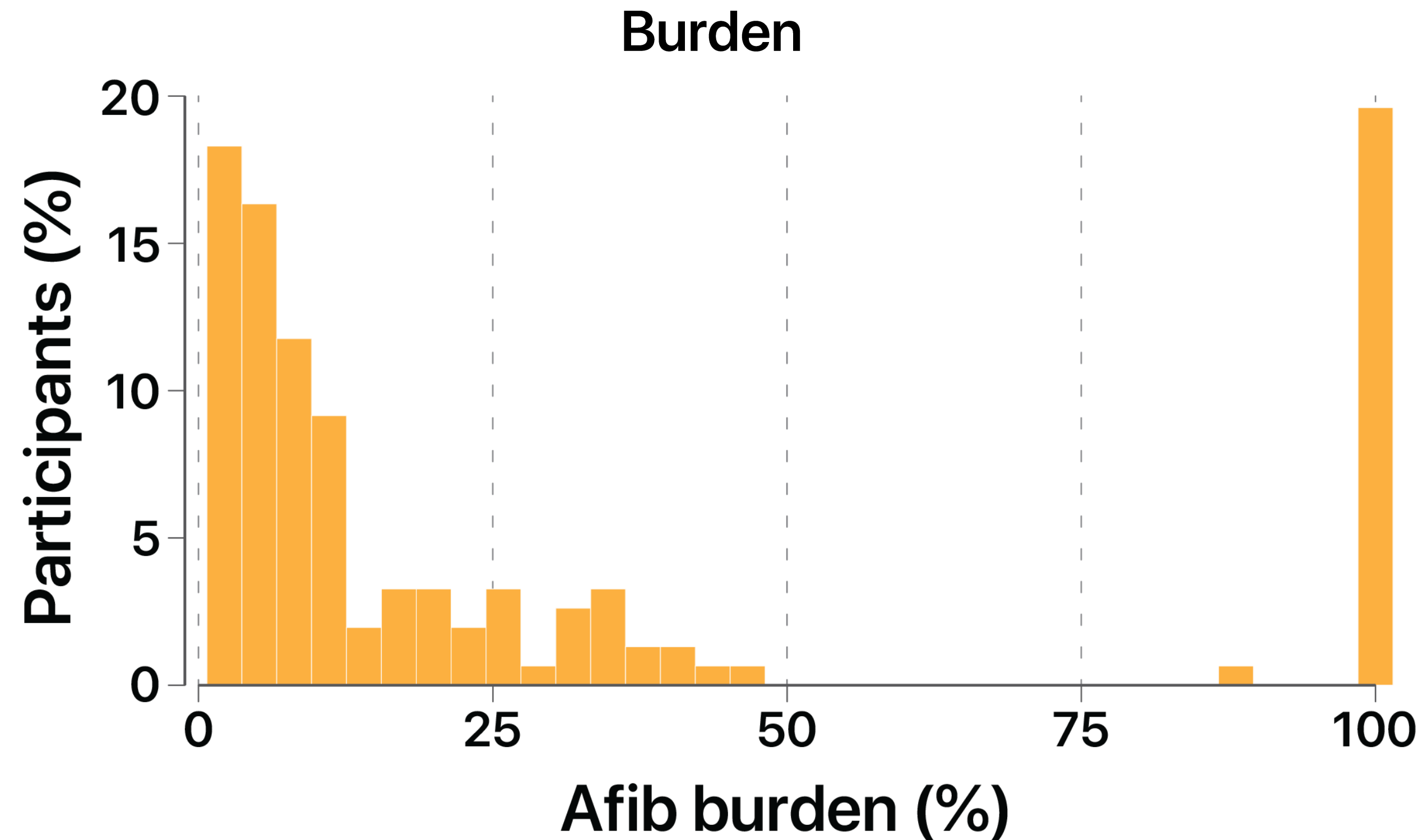
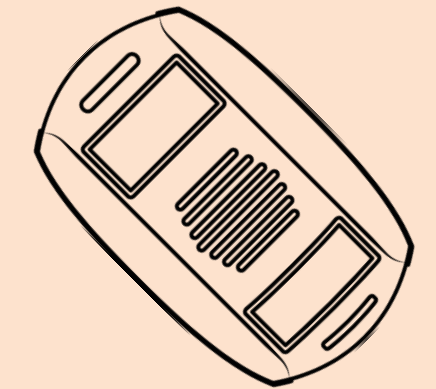
| | Afib on ECG Patch | Positive Tachograms | PPV* (97.5% CI) |
|----------|-------------------|---------------------|--------------------|
| Overall | 1,489 | 2,089 | 0.71 (0.69–0.74) |
| Age ≥ 65 | 548 | 914 | 0.60 (0.56 – 0.64) |

| | Afib on ECG Patch | Positive Notifications | PPV (95% CI) |
|----------|-------------------|------------------------|--------------------|
| Overall | 72 | 86 | 0.84 (0.76–0.92) |
| Age ≥ 65 | 25 | 32 | 0.78 (0.64 – 0.92) |



Afib Burden and Duration

ECG Patch
153/450 With AF



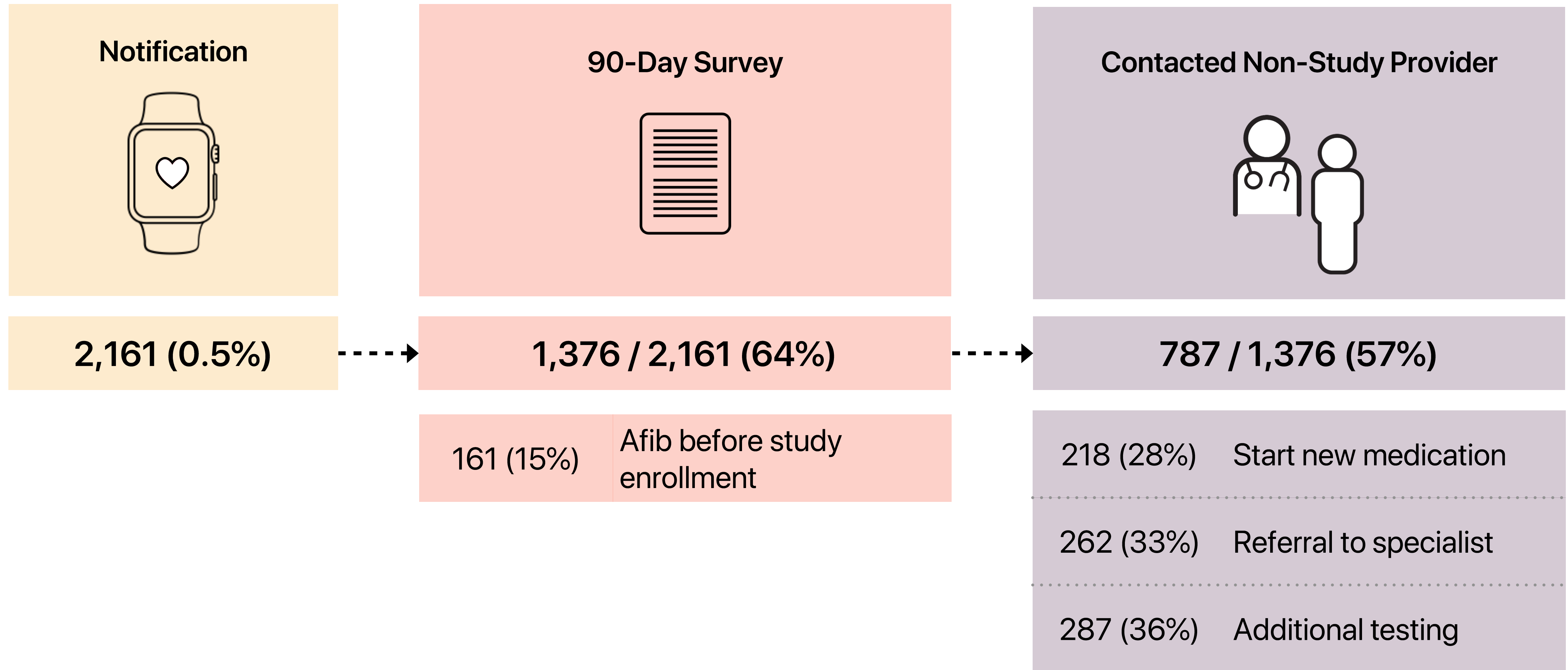
Duration of Longest Episode

| | |
|--------|-------|
| 24 hr | 25.5% |
| 6 hr | 34.0% |
| 1 hr | 29.4% |
| 6 min | 5.9% |
| 30 sec | 5.2% |


89%



90-Day Survey



Adverse Events

| | Overall Cohort  n =419,297 |
|--------------------------------|---|
| Total | 1038 |
| Not related to App | 1022 |
| Serious | 71 |
| Non-serious, expected | 141 |
| Non-serious, unexpected | 810 |
| Related to App | 16 |
| Serious | 0 |
| Non-serious, expected | 14 |
| Non-serious, unexpected | 2 |



Limitations

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



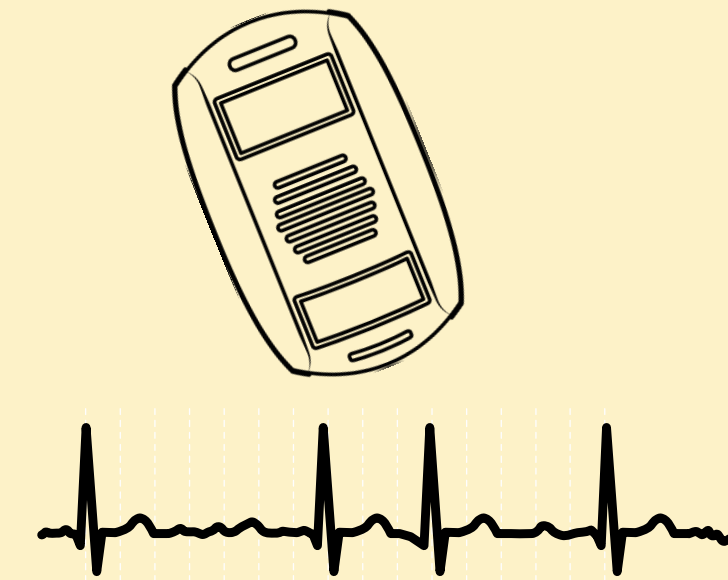
Conclusions



Study w/ Novel Virtual Design
419,297 in 8 months



Proportion Notified low
Overall: 0.52% (0.49-0.54)



ECG patch 13 days after
34% had Afib



Positive predictive value
Tachogram: 0.71 (0.69-0.74)
Notification: 0.84 (0.76-0.92)



57% Notified (surveyed)
Contacted Non-Study Provider



Exposure to the
app was safe



Clinical Implications

- In the AHS, we found a low proportion of notifications across a diverse population
- Notification PPV of 0.84 supports ability to correctly identify Afib among those notified
- Findings may inform further clinical evaluation after notification (with history, exam)
- Future Direction: Rigorous investigation of this technology and its potential use in clinical setting.
- AHS provides solid foundation upon which further research in digital health can be conducted.



Study Organization



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TeleHealth provider

American Well[®]

Ambulatory ECG provider

BioTelemetry
inc



**Thank you to all
of our participants**

