

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

# The Apple Heart Study



Mintu Turakhia MD MAS and Marco Perez MD  
*on behalf of the Apple Heart Study Investigators*

NCT # 03335800

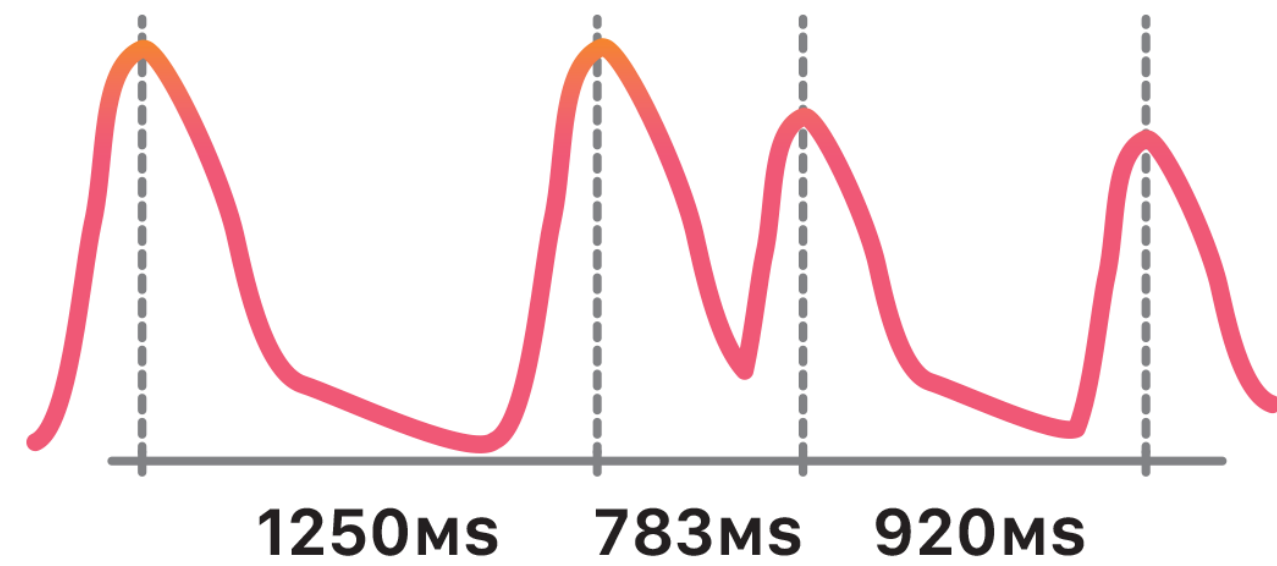


# Introduction

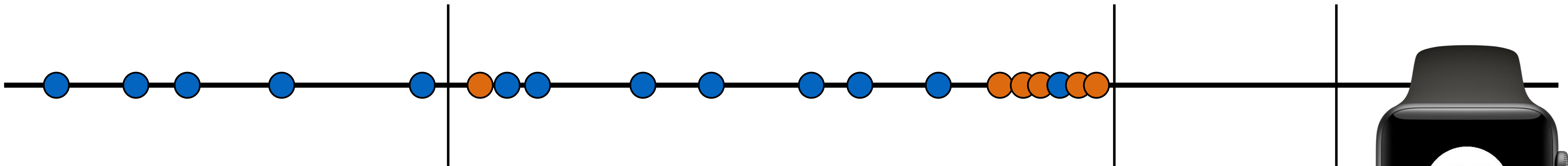
- Optical sensor detects pulse waveform passively to measure heart rate
- Detection of pulse irregularity may be useful to identify atrial fibrillation ("Afib")



# Irregular Pulse Notification Algorithm



- Algorithm results
- Regular pulse
  - Suggestive of Afib



Tachogram = Periodic spot measurements

5 confirmations  $\Rightarrow$  notify user

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



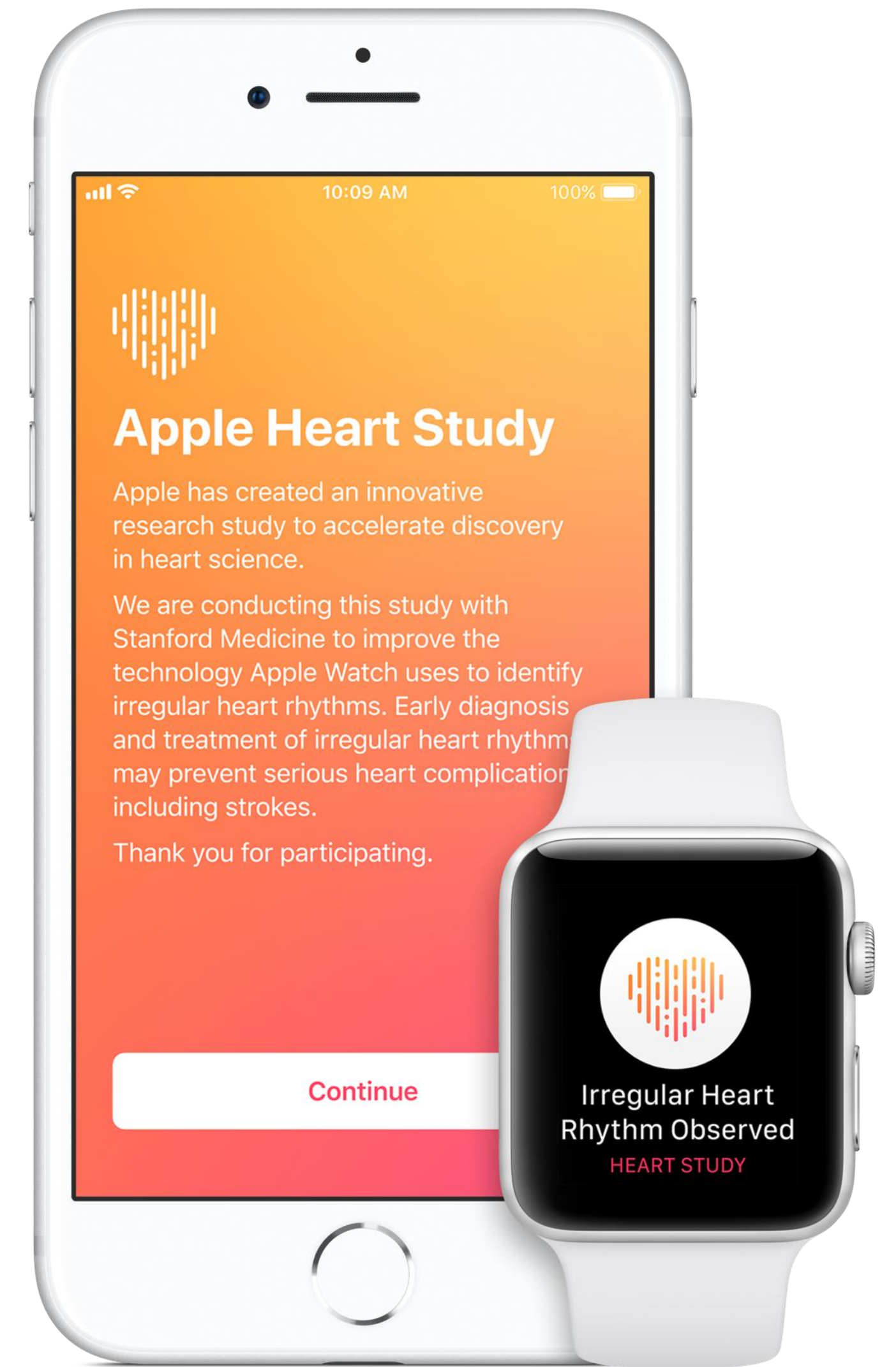
The algorithm does not use the watch ECG feature



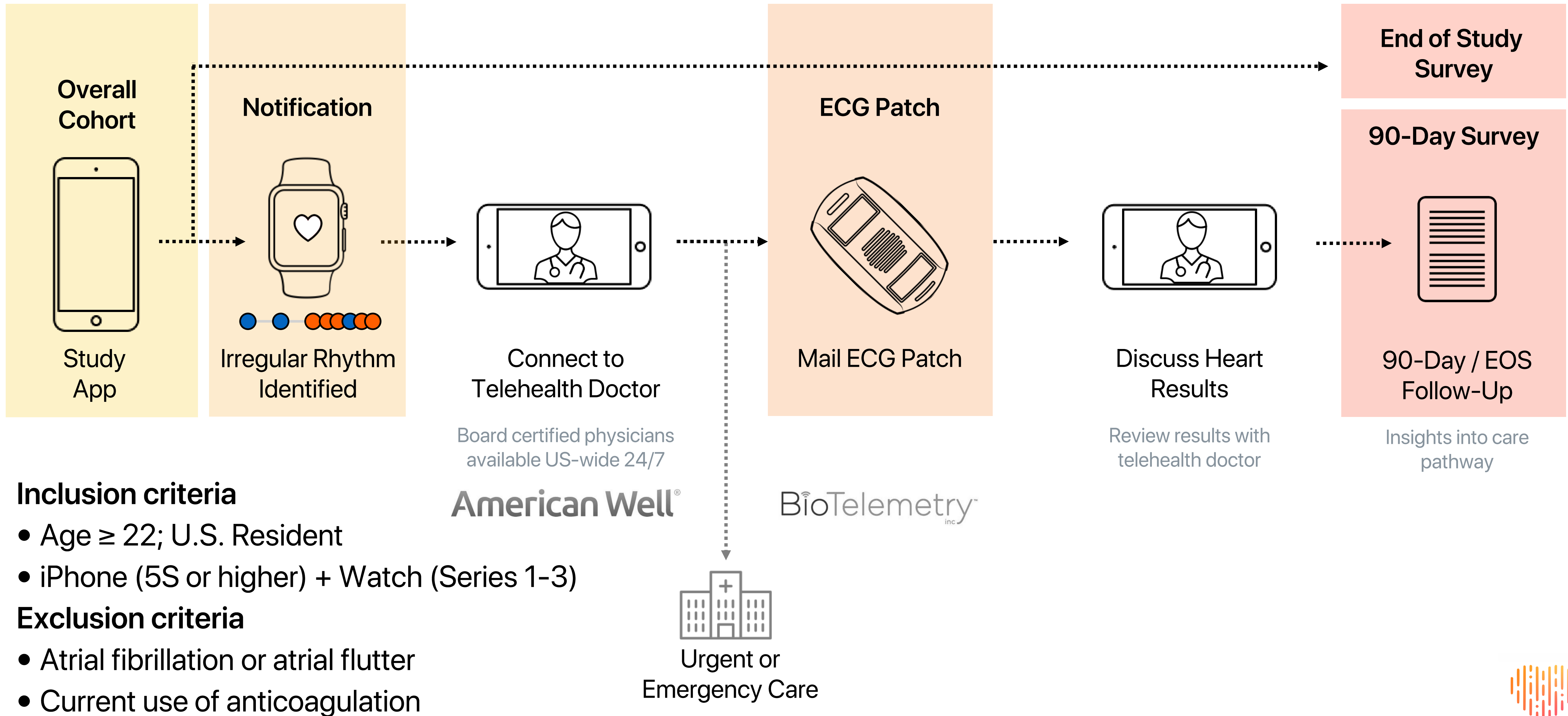
# Overall Goal

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

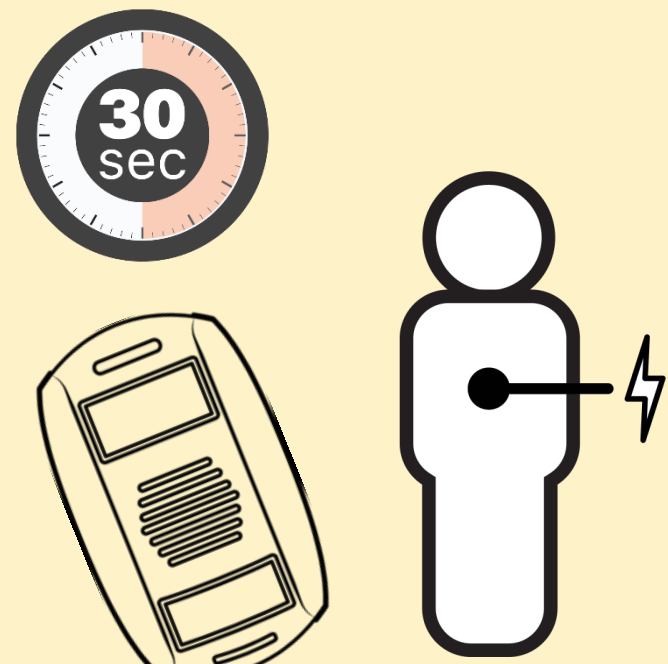


# Prospective, Single Arm, Open Label, Non-Significant Risk Study

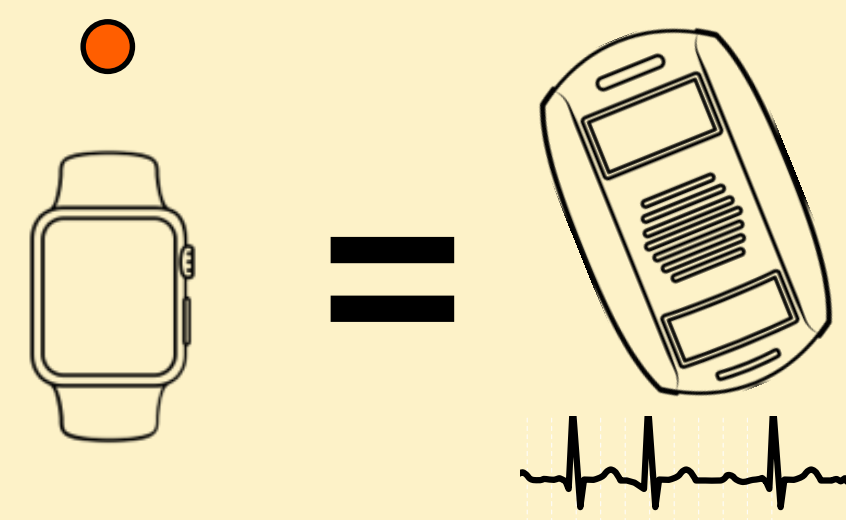


# Primary Endpoints

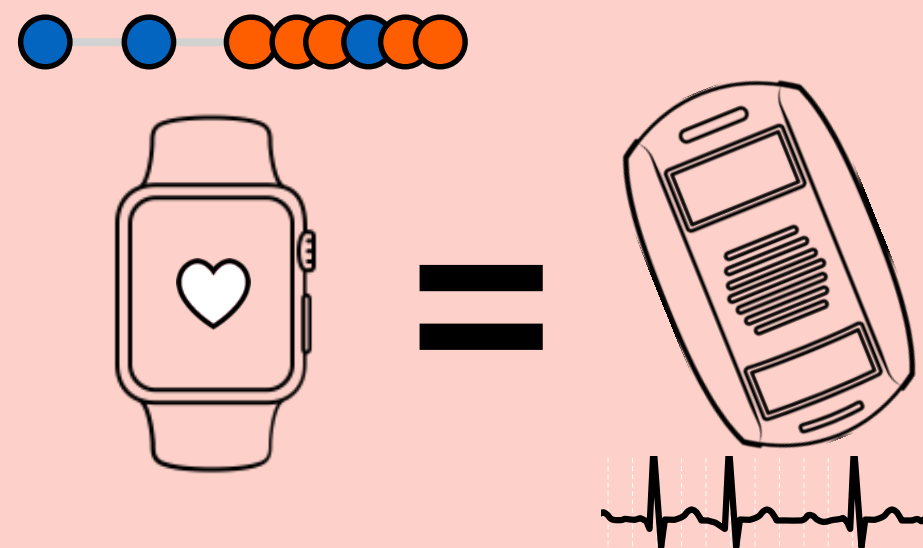
# Secondary Endpoints



Afib > 30 seconds  
on ECG patch  
in patients  $\geq$  65 years



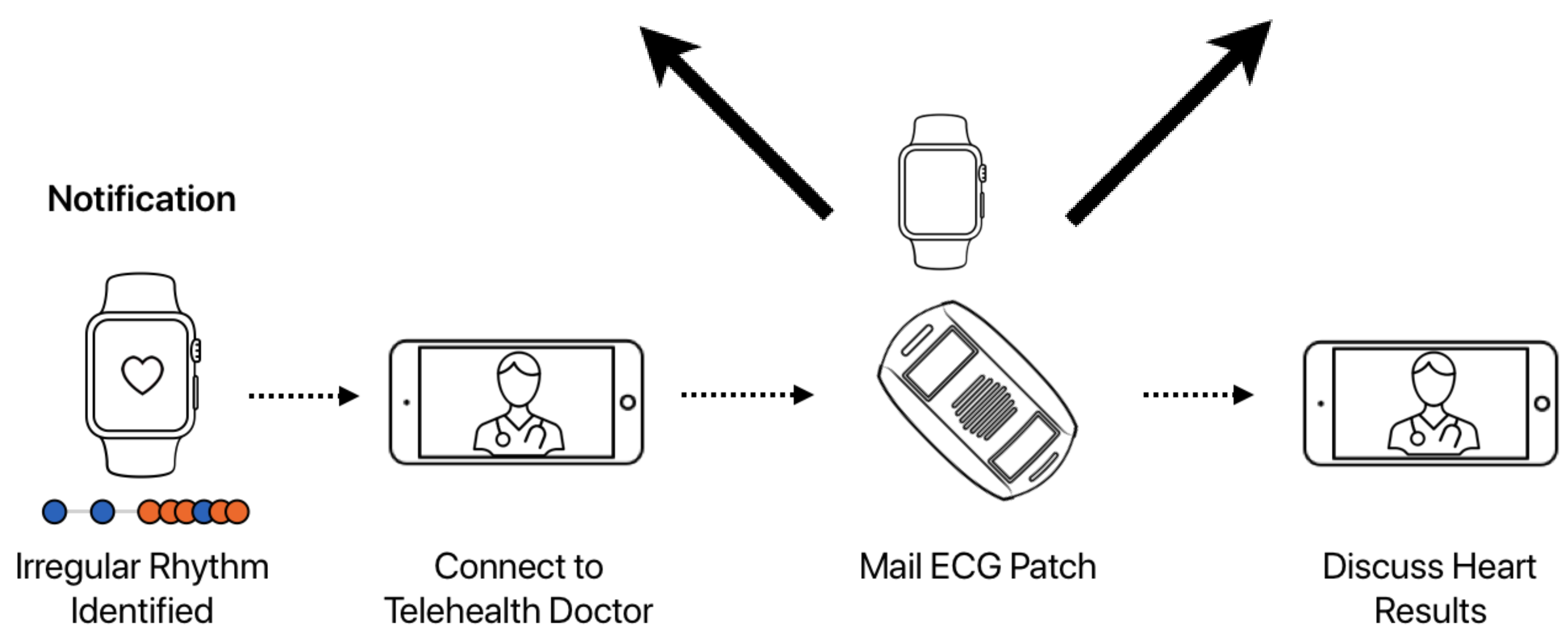
Simultaneous Afib on  
ECG Patch and  
individual tachogram



Simultaneous Afib on  
ECG Patch w/ notification



Self-reported contact  
w/ health care provider

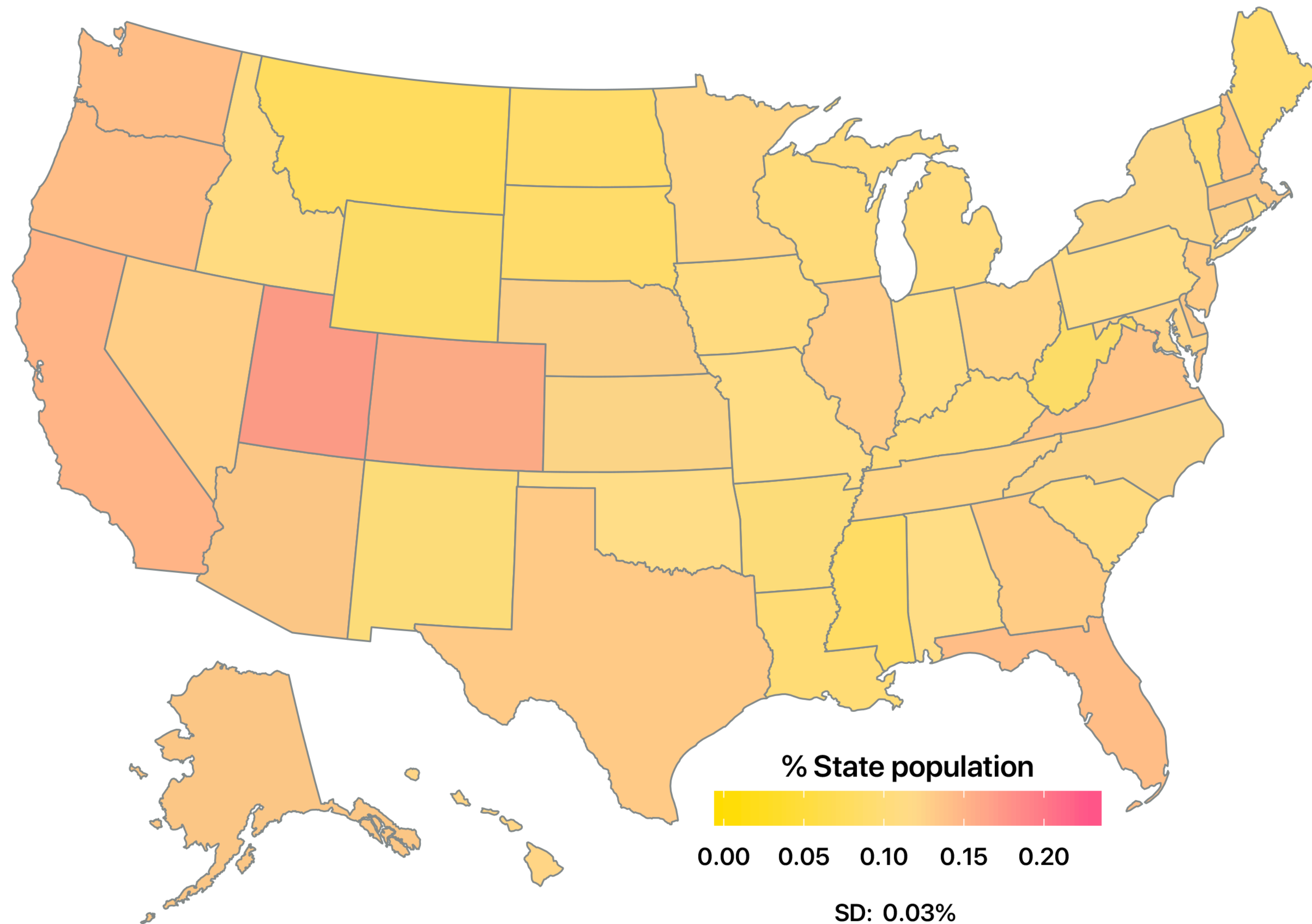


# Statistical Considerations

- Single-arm study with an enrollment goal of up to 500,000
  - Assumption was to have 503 patches in age  $\geq 65$  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  $\geq 65$  and  $< 65$
  - The positive predictive value or *PPV of an individual tachogram with simultaneous ECG patch*
    - 97.5% CI lower bound  $>0.70$  and upper bound  $\geq 0.75$



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



**Enrollment:**  
Nov 29, 2017 – Jul 31, 2018

**Last data collection:**  
Feb 25, 2019

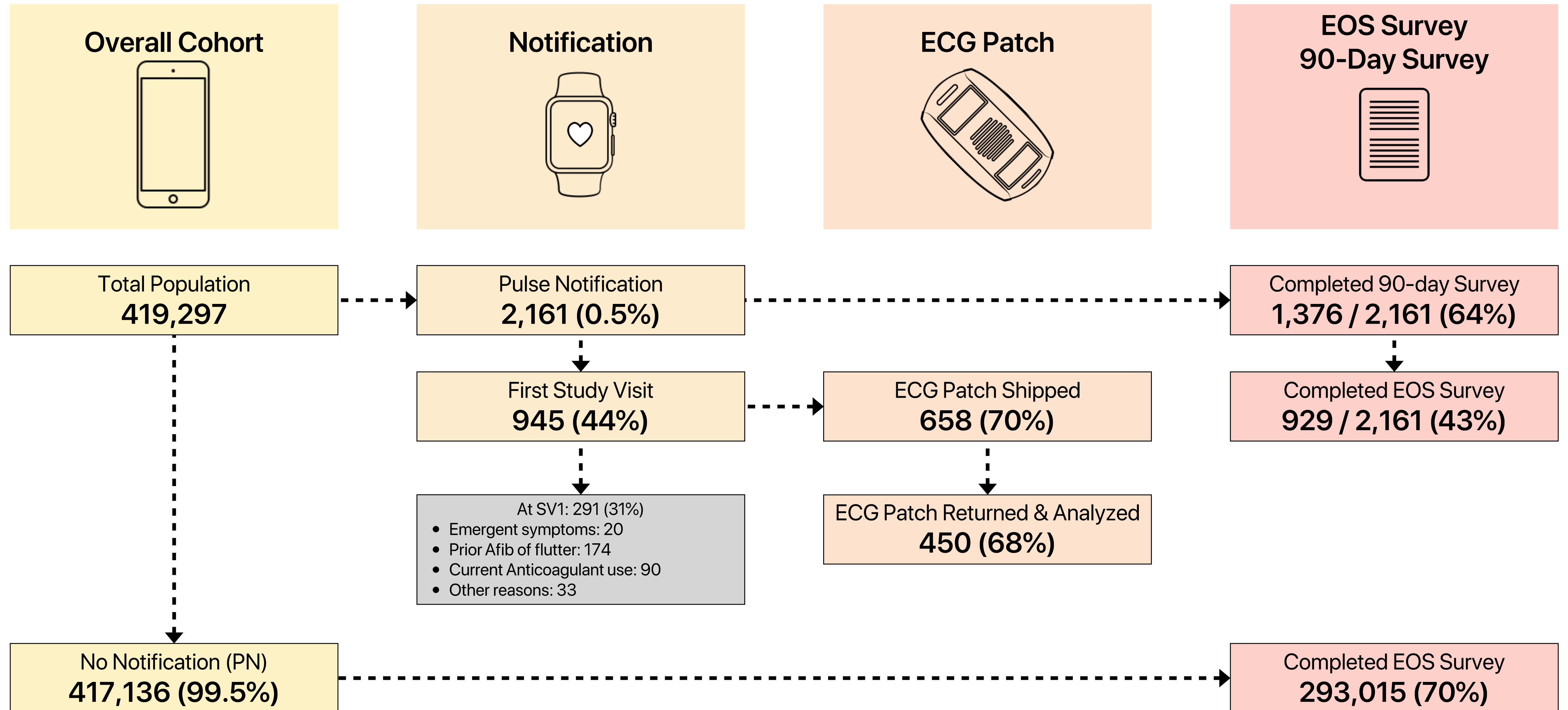
**% State population**  
0.00 0.05 0.10 0.15 0.20

SD: 0.03%  
Mean: 0.12%

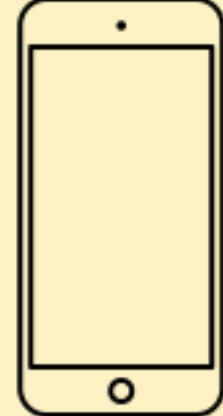

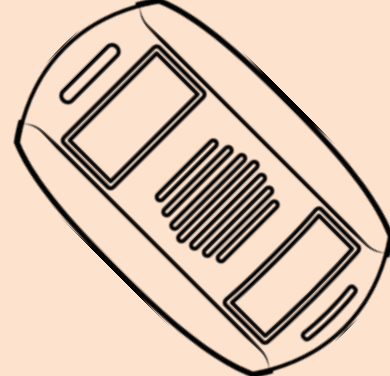




# Consort Diagram



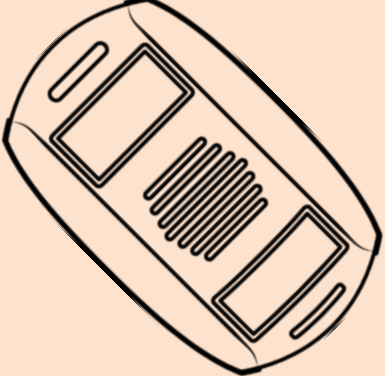


# Baseline Demographics

		Overall Cohort 	Notification 	ECG Patch 
	N	419,297	2,161	450
	Female (%)	177,087 (42)	461 (21)	102 (23)
Age	Age, mean (sd)	40.81 (13)	56.86 (15)	58.63 (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 <sub>2</sub> DS <sub>2</sub> 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

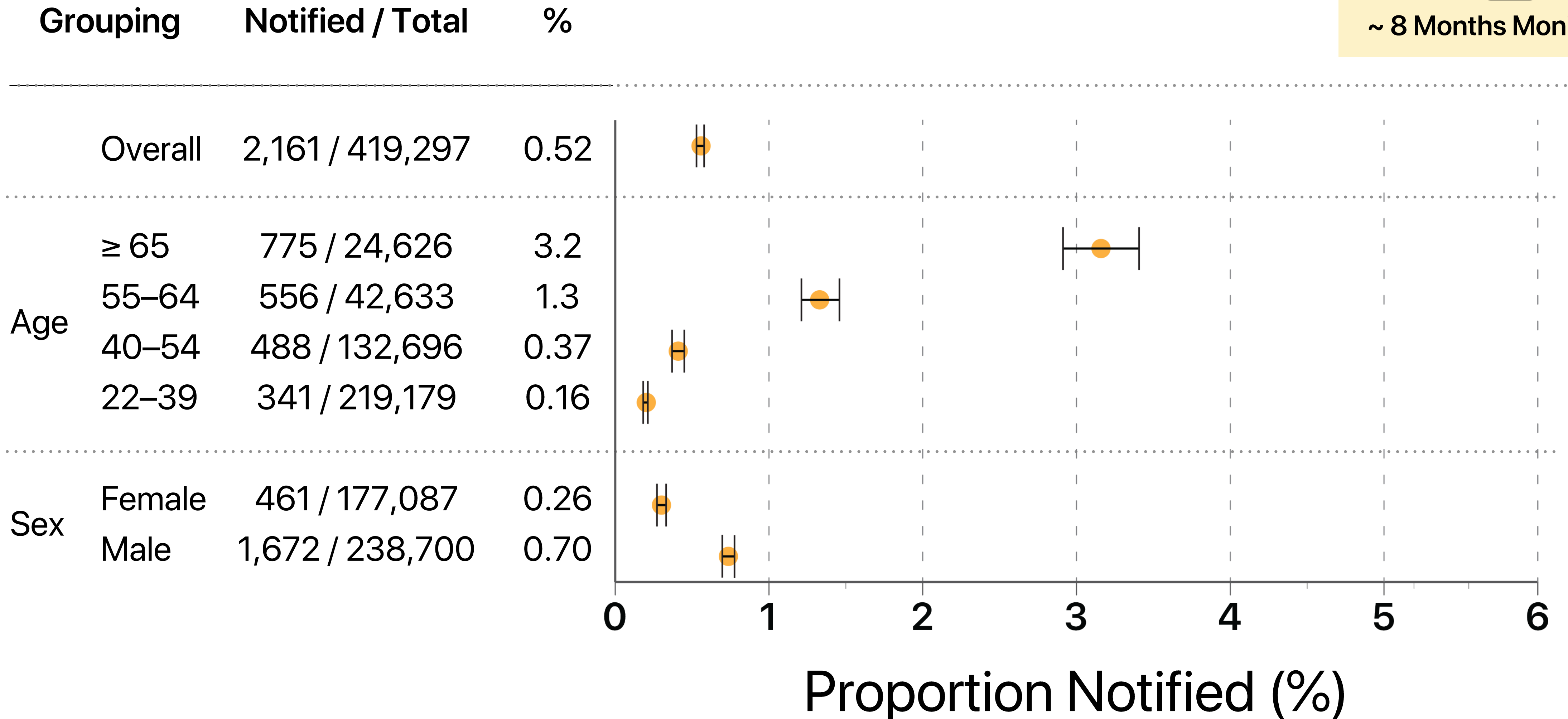


# Initial Irregular Pulse Notifications

Overall Cohort

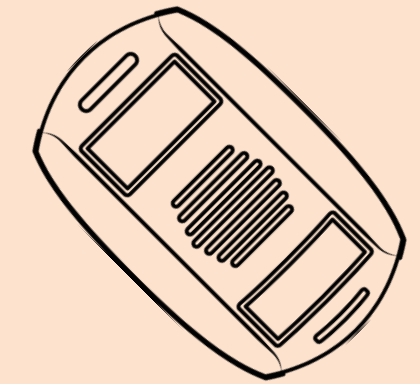


~ 8 Months Monitoring

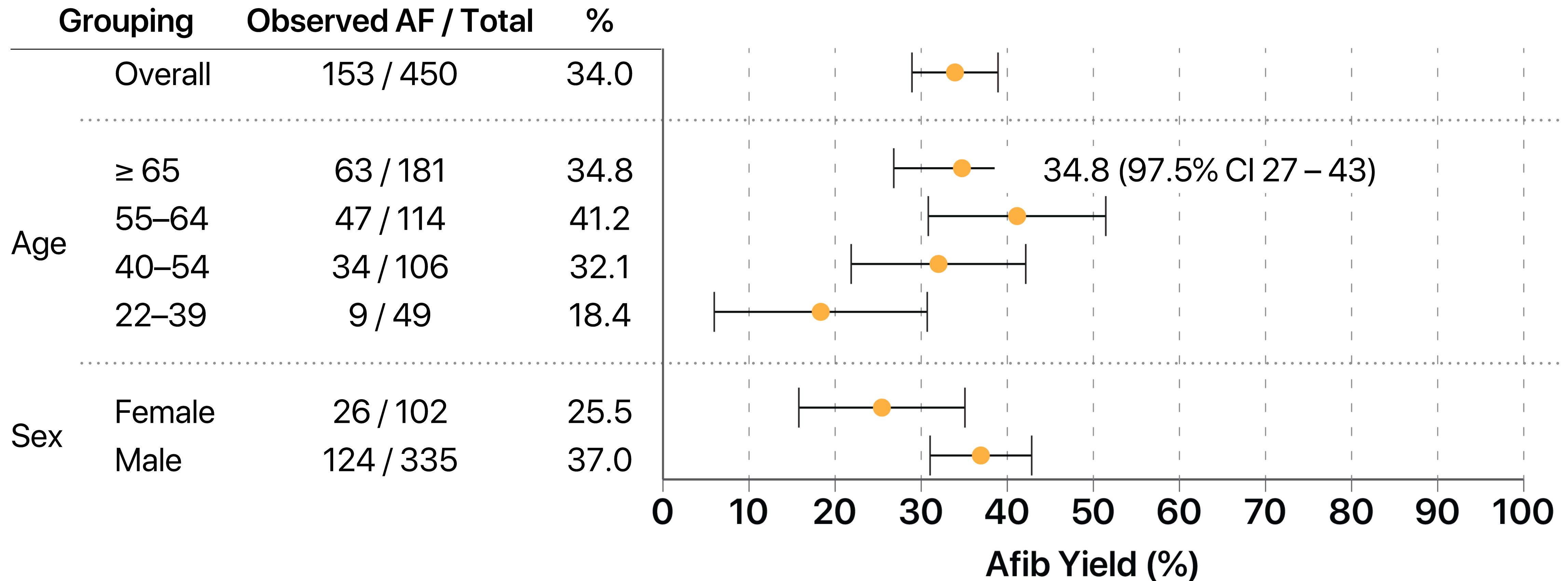


# Afib Yield on ECG Patch

ECG Patch (450/2,161)

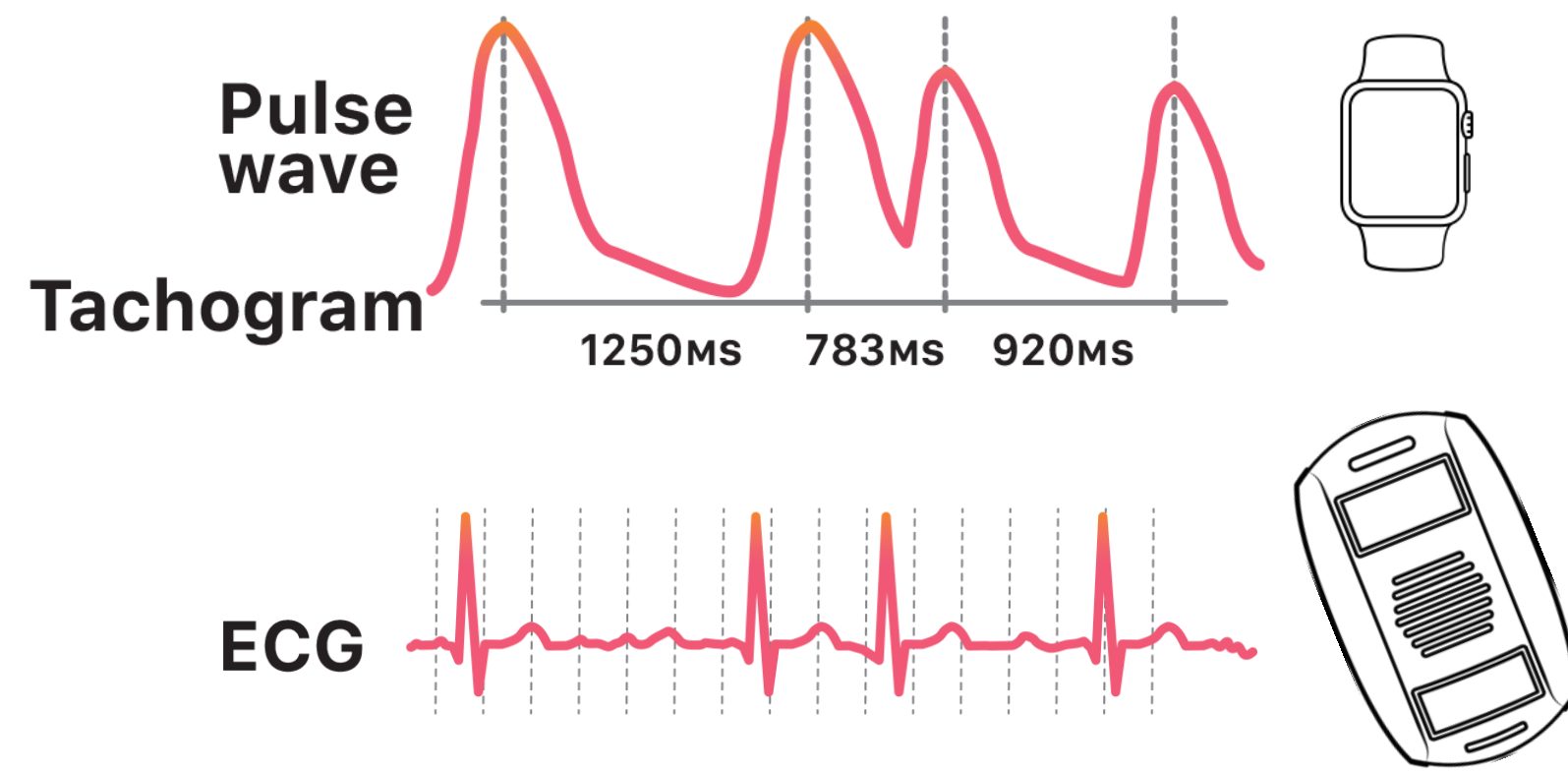


Mean time to hookup: 13 days  
Mean wear time: 6.3 days

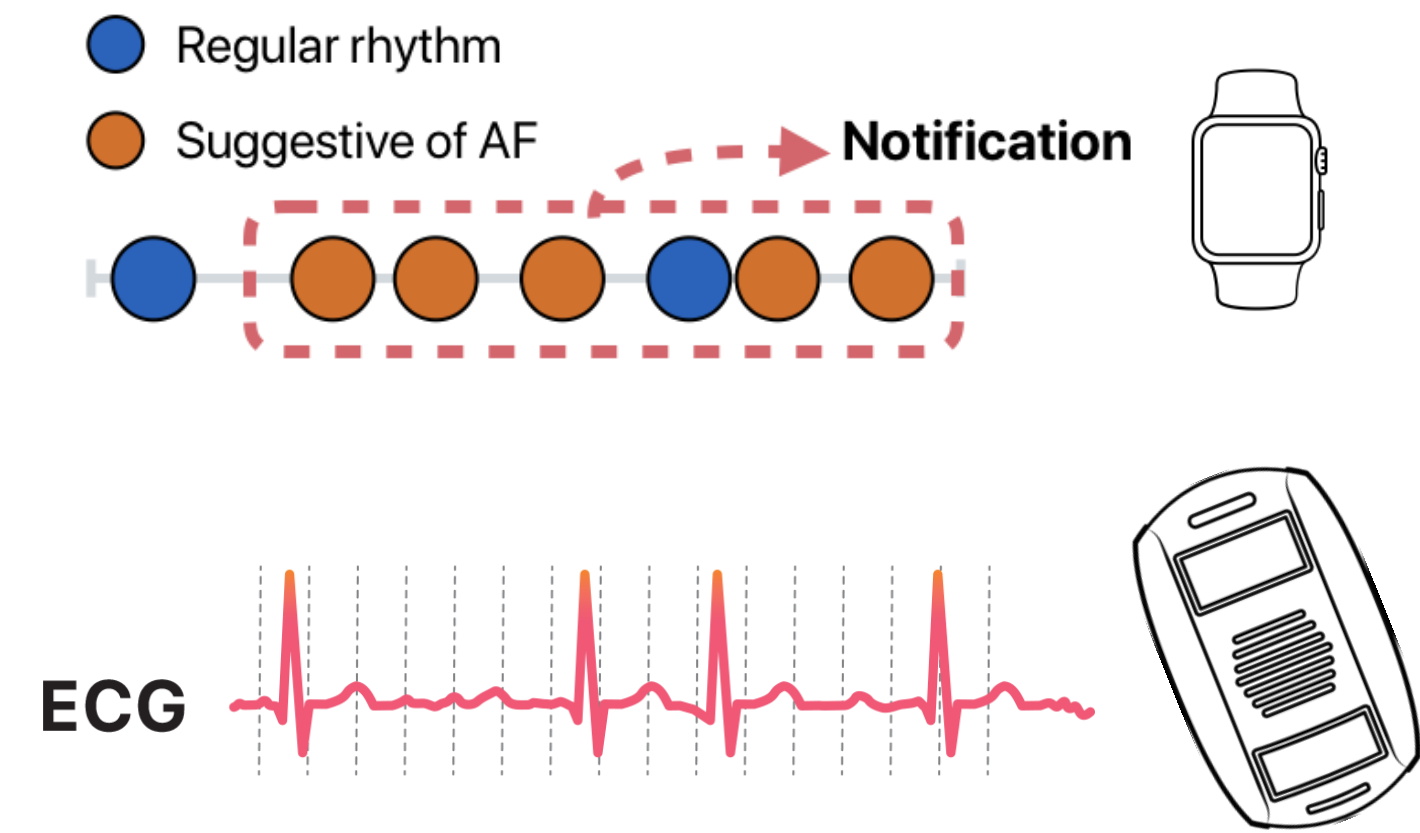


# Positive Predictive Values

## Irregular Tachograms



## Irregular Pulse Notifications



Afib on ECG Patch	Total Positive Tachograms	PPV* (97.5% CI)
1,489	2,089	0.71 (0.69–0.74)

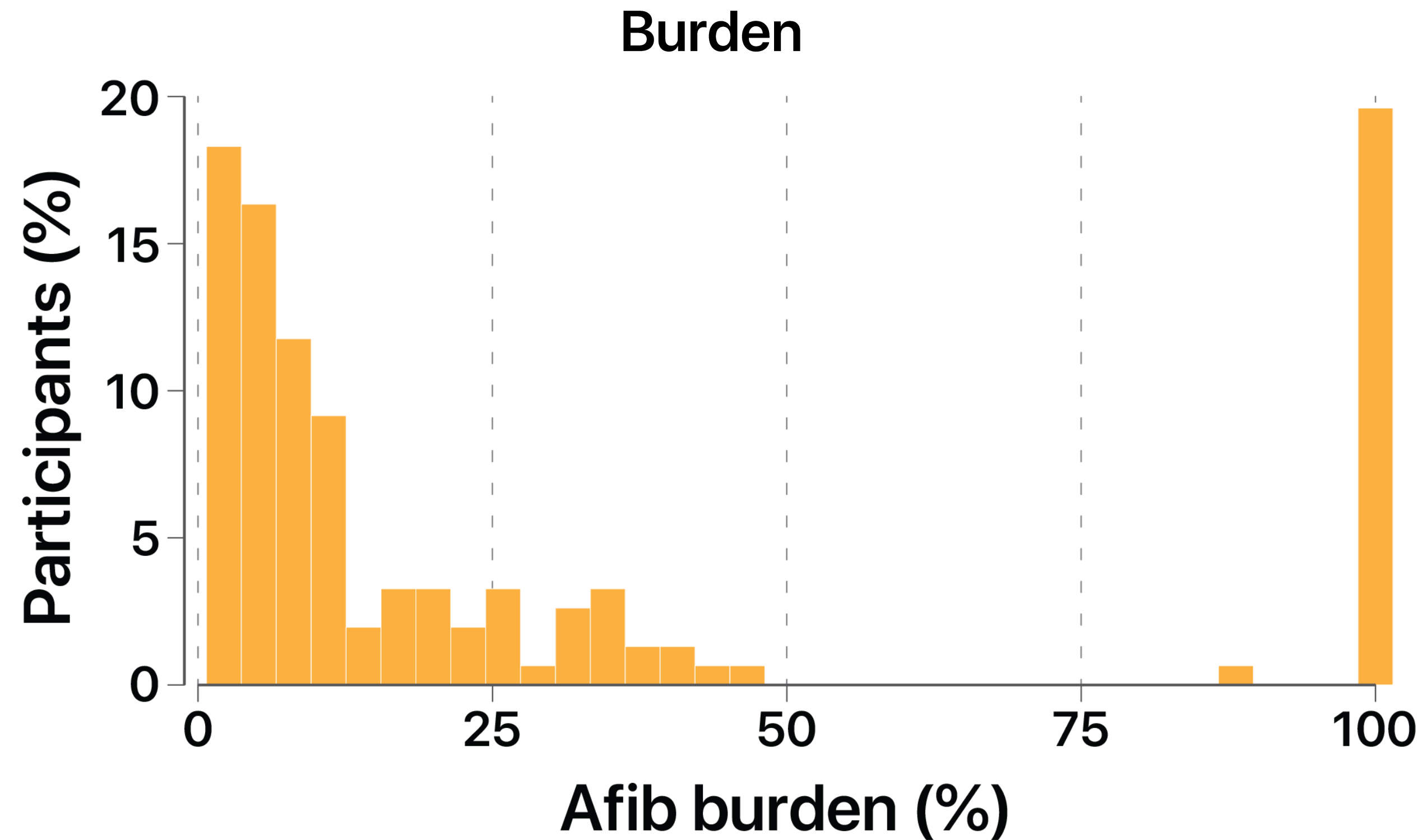
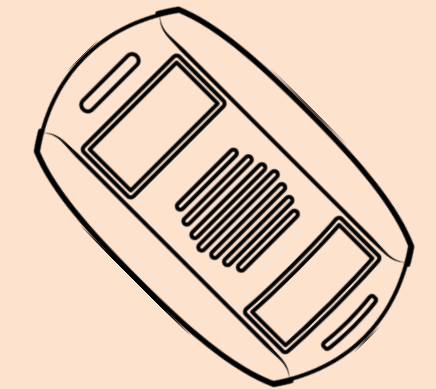
Afib on ECG Patch	Total Positive Notifications	PPV (95% CI)
72	86	0.84 (0.76–0.92)

\* Decision rule for lower bound of CI  $\geq 0.7$  and upper bound  $\geq 0.75$  not met



# Afib Burden and Duration

ECG Patch  
153/450 With AF



### Duration of Longest Episode

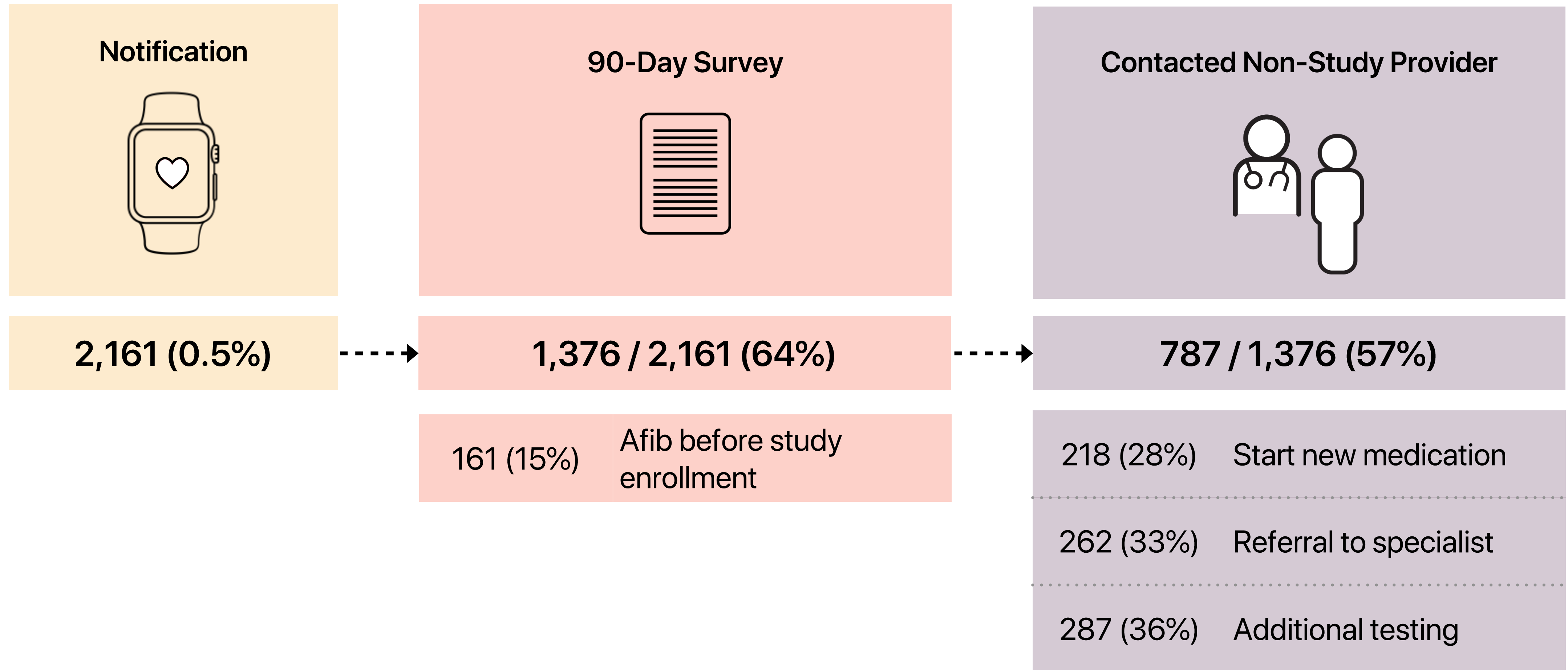
24 hr	25.5%
6 hr	34.0%
1 hr	29.4%
6 min	5.9%
30 sec	5.2%

**89%**






# 90-Day Survey



# Adverse Events

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



# Limitations

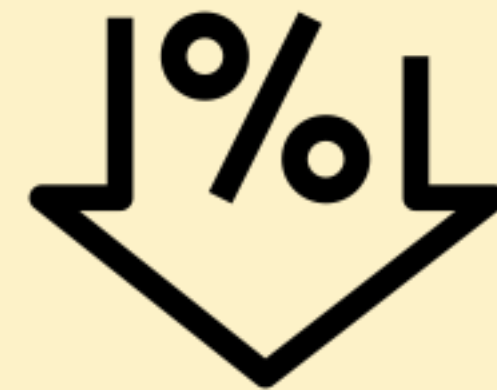
- Pre-specified precision of co-primary endpoints not achieved
  - Confidence intervals presented reflect measured uncertainty
- Virtual Study Design (large, quick, pragmatic)
  - Self-assessment of enrollment criteria
  - Self-reported outcomes
- Higher than anticipated drop offs after notification
  - Fewer than anticipated telehealth study visits
  - Fewer than anticipated ECG patches



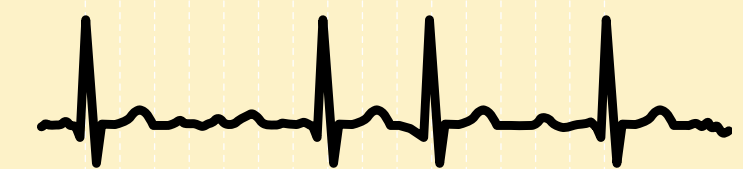
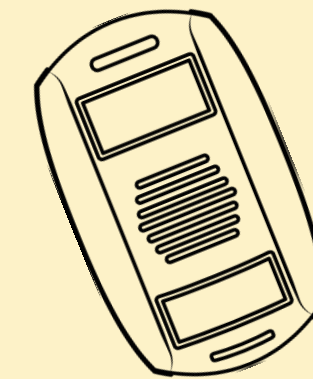
# Conclusions



Operational success  
419,297 in 8 months



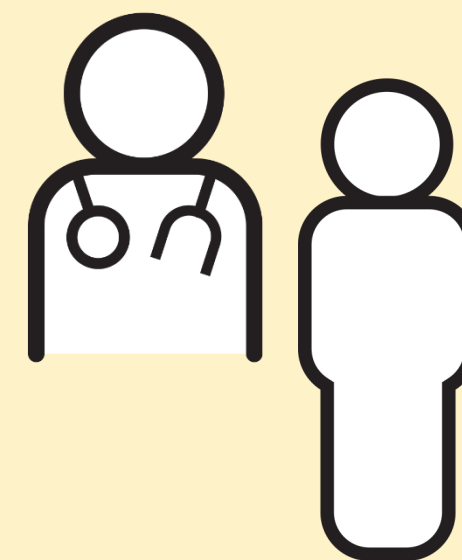
Irregular pulse notification  
rates were low  
Overall: 0.52% (0.49-0.54)



ECG patch 13 days later  
34% had Afib



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



Contact Non-Study Provider  
within 90 days : 57%



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



**Stanford Center for Clinical Research**  
Nisha Talati, Karma Lhamo, Shea Smith

**Quantitative Sciences Unit**  
Haley Hedlin, Ariadna Garcia,  
Vidhya Balasubramanian

**Center for Digital Health**  
Mariam Askari, Avani Gupta

**Information Resources & Technology**  
Todd Ferris, Grace Hung, Don Mitchell

## Steering Committee

Ken Mahaffey (chair), Mintu Turakhia (co-PI),  
Marco Perez (co-PI), Deidre Caldbeck, Lauren Cheung,  
Manisha Desai, Sumbul Desai, Danielle Dorfman,  
Chris Granger, Peter Kowey, Divya Nag, Amol Rajmane,  
John Rumsfeld, Andrea Russo, Mellanie True Hills

## Data Safety Monitoring Board

### Duke Clinical Research Institute

Frank Rockhold (chair), Christine Albert, Alvaro Alonso,  
Lisa Wruck

## Safety Desk and Clinical Support

Connor O'Brien, Alex Perino, Justin Parizo, Christoph  
Olivier, Mai Nguyen, Sushmitha Tallapalli, Rajvir Kaur

## Ambulatory ECG adjudicators

Chad Brodt, Lee Chang, Paul Cheng, Julie Dong,  
Karen Friday, Ronald Jones, Petra Mamic, David Ouyang,  
Shirley Park, AJ Rogers, Rajan Shah, Matthew Wheeler,  
Alberta Yen, Peem Lorvidhaya



## Sponsor

Christine Toruno, Alexis Beatty,  
Jeff Stein, Steve Waydo

## TeleHealth provider

**American Well**<sup>®</sup>

## Ambulatory ECG provider

**BioTelemetry**  
inc



**Thank you to all  
of our participants**

