3-year Clinical Outcomes in a Nationwide Pragmatic Clinical Trial Of Atrial Fibrillation Screening - mHealth Screening To Prevent Strokes (mSToPS)

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Scripps Research Translational Institute

#AHA20 November 16, 2020

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Background

- For adults over age 55, the lifetime risk of developing AF is nearly 40%.[1]
- AF is associated with ~32% of all strokes in high-income countries.[2]
- Once AF is recognized, therapeutic anticoagulation can decrease the risk of stroke by ~65% & mortality by ~30%.[3]
- For 20-50% of individuals with AF and stroke, AF is first diagnosed around the time of the stroke.[4,5]
  - AF is paroxysmal in 87%
  - AF diagnosed at the time of stroke was more common in younger individuals free of other cardiovascular disease (i.e low CHADS-VASc)

1. Weng LC. *Circulation.* 2018;137:1027-1038. 2. Perera KS. Stroke. 2016;47:2197-2202 3. Freedman B. Lancet 2016;388:806–17
4. Jaakkola J. PLoS ONE 2016;11:e0168010. 5. Yao X. Am Heart J 2018;199:137-43

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Key Objectives

MSToPS

1. In the context of a digital clinical trial, determine if participant-generated data available through a wearable ECG patch can improve the identification of AF relative to routine care.

2. **To determine if screening for atrial fibrillation by wearing an ECG patch can improve clinical outcomes at 3 years after the initiation of screening.**

Methods

Direct-to-Participant, Siteless Design

aetna® Members

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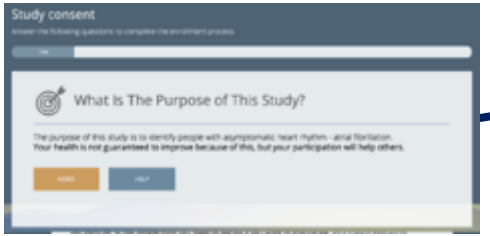
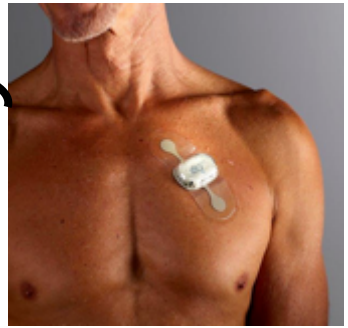
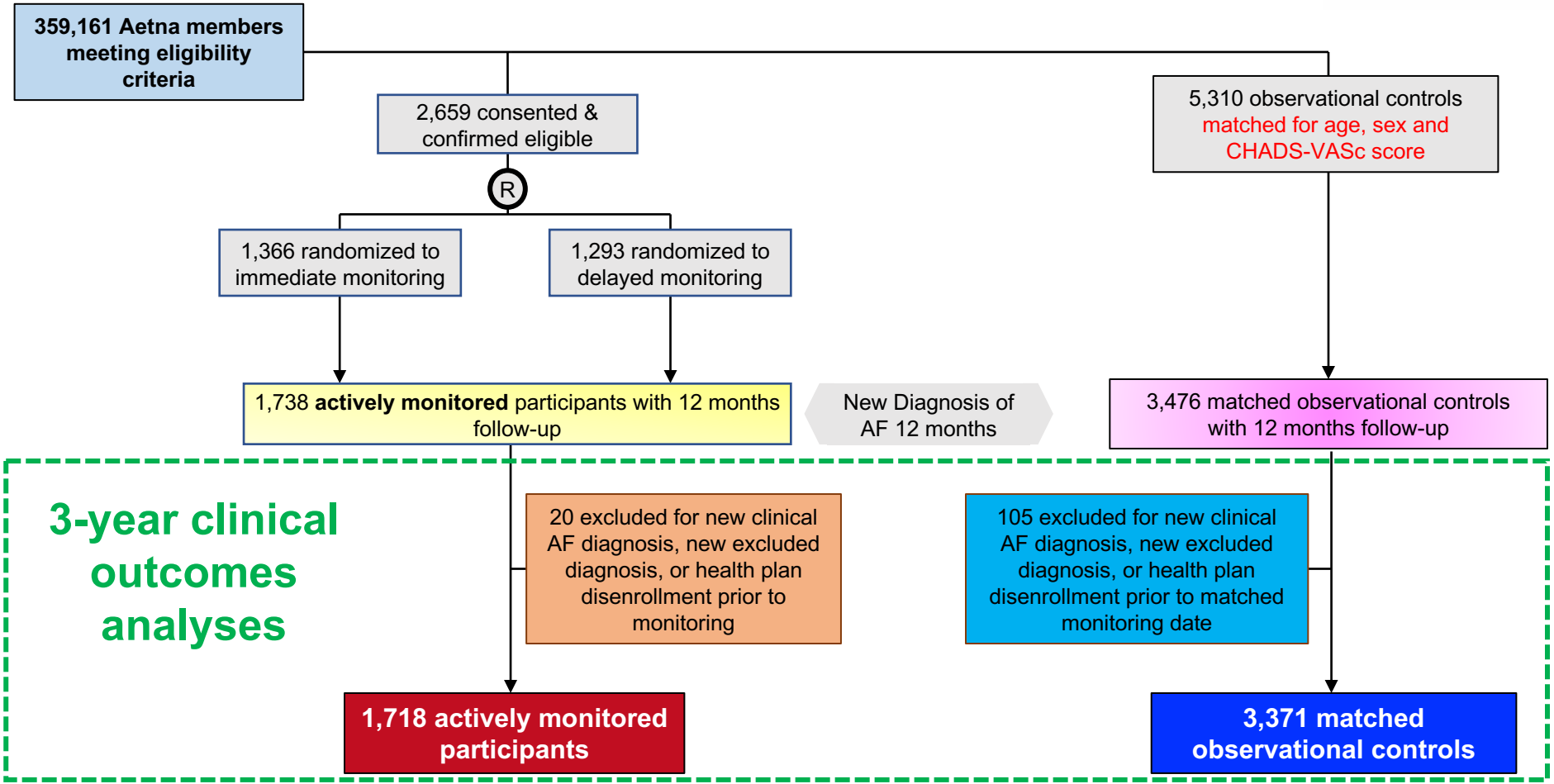
Median total monitoring time of 24.7 days





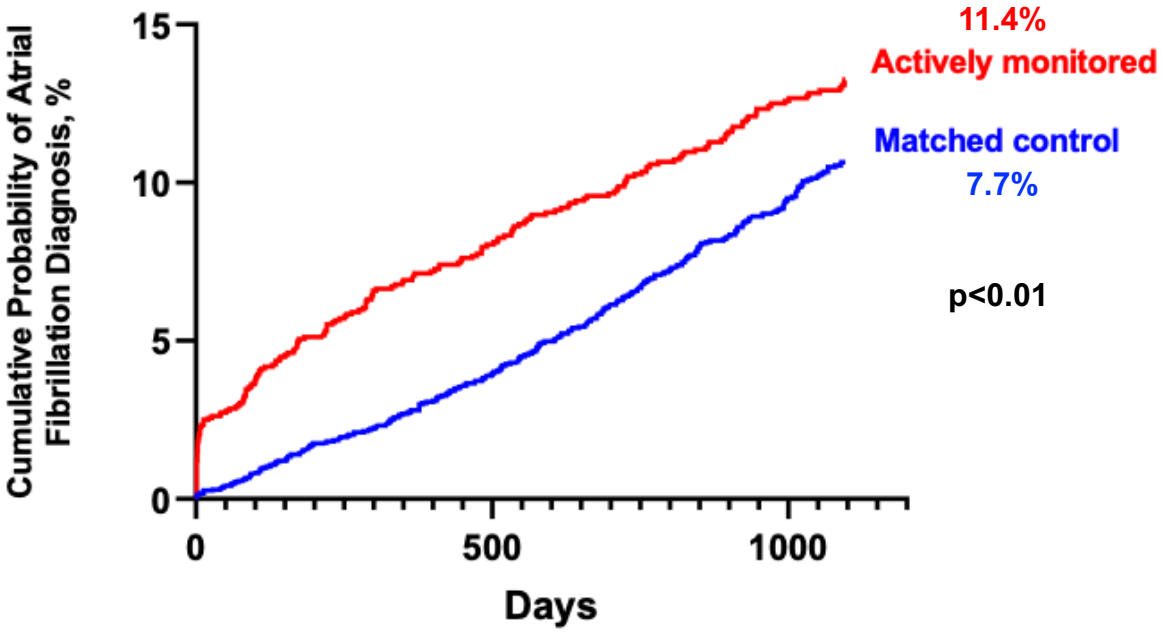
JAMA. 2018;320(2):146-155.


359,161 Aetna members meeting eligibility criteria
2,659 consented & confirmed eligible
R
1,366 randomized to immediate monitoring
1,293 randomized to delayed monitoring
5,310 observational controls matched for age, sex and CHADS-VASc score
1,738 actively monitored participants with 12 months follow-up
New Diagnosis of AF 12 months
3,476 matched observational controls with 12 months follow-up
3-year clinical outcomes analyses
20 excluded for new clinical AF diagnosis, new excluded diagnosis, or health plan disenrollment prior to monitoring
105 excluded for new clinical AF diagnosis, new excluded diagnosis, or health plan disenrollment prior to matched monitoring date
1,718 actively monitored participants
3,371 matched observational controls

Prespecified 3-Year Primary Outcomes

- Time to first event of the combined endpoint of death, stroke, systemic embolism, or myocardial infarction via claims and membership data among-
  - Those with a diagnosis of AF at any time during the pre-specified 3-year analysis period, and
  - **The entire cohort.**
- The primary safety endpoint was the incidence rate of hospitalization for a primary bleeding diagnosis.

Time to First Diagnosis of Atrial Fibrillation



- For the actively monitored cohort:
  - 32% diagnosed by patch
  - 68% clinically
- In those with pharmacy data available, anticoagulants were initiated in 45.2% of controls and 44.0% of actively monitored cohort. (p=0.84)

Baseline Demographics

	Actively Monitored Arm (n=1718)	Observational Control Arm (n=3371)	P-Value
Age (years), mean (SD)	73.8 (7.0)	73.7 (7.0)	*
Female, n (%)	699 (40.7%)	1374 (40.8%)	*
CHA_2DS_2 VASc Score, median (Q1-Q3)	3 (2-4)	3 (2-4)	*
Stroke, n (%)	218 (12.7%)	323 (9.6%)	<0.01
Heart Failure, n (%)	84 (4.9%)	196 (5.8%)	0.17
Hypertension, n (%)	1290 (75.1%)	2597 (77.0%)	0.12
Diabetes Mellitus, n (%)	598 (34.8%)	1195 (35.5%)	0.65
Sleep Apnea, n (%)	459 (26.7%)	700 (20.8%)	<0.01
Prior Myocardial Infarction, n (%)	91 (5.3%)	230 (6.8%)	0.03
Chronic Obstructive Pulmonary Disease, n (%)	137 (8.0%)	341 (10.1%)	0.01
Obesity, n (%)	288 (16.8%)	601 (17.8%)	0.34
Chronic Renal Failure, n (%)	182 (10.6%)	305 (9.0%)	0.08

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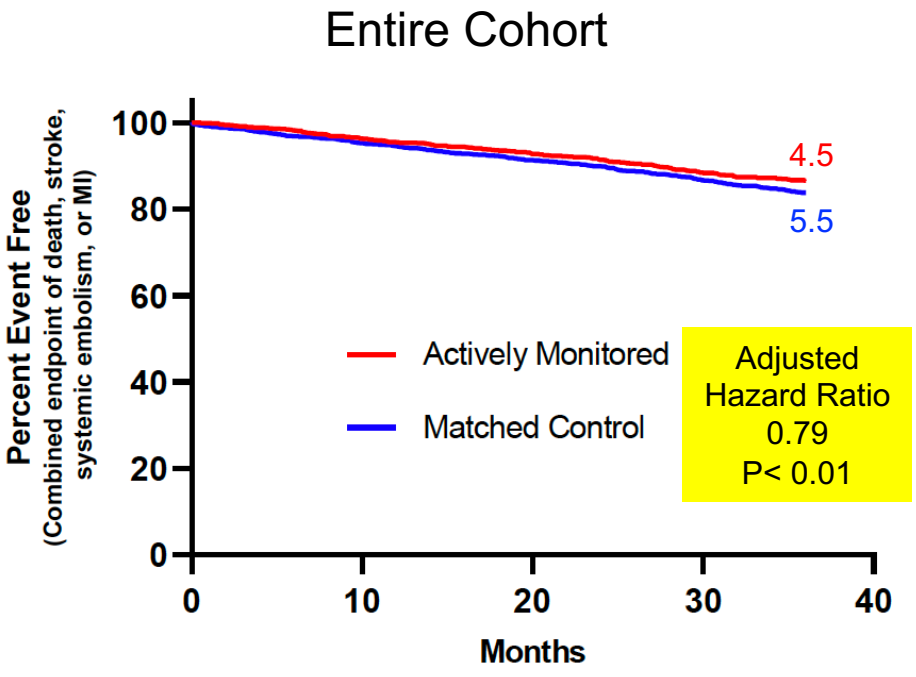
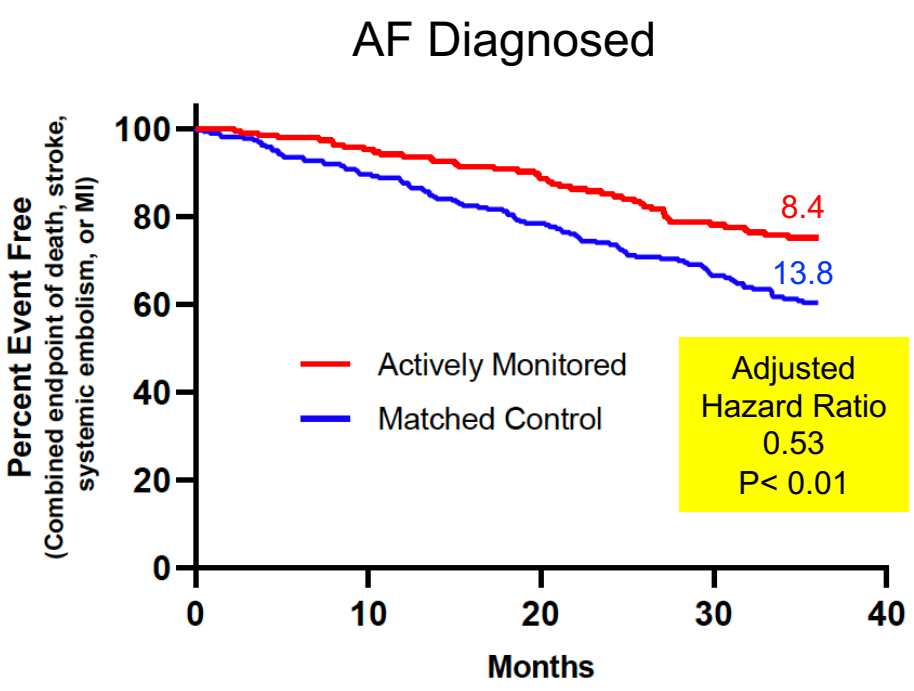
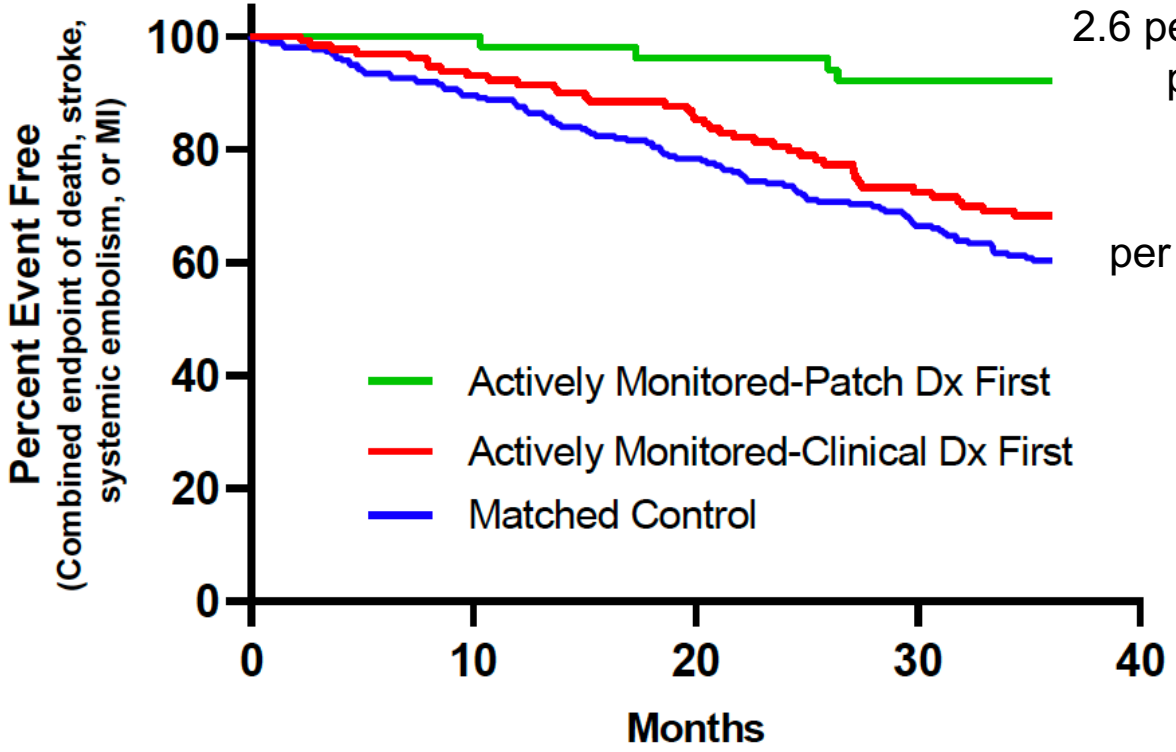
Primary Combined Endpoint
Death, Stroke, MI or Systemic Emboli





Mean duration of eligible follow-up - 29 months

Primary Combined Endpoint in AF-Diagnosed Based on How Diagnosed



2.6 per 100 person-years
p<0.01 for both

10.9 vs 13.8
per 100 person years
p=0.21

Entire Cohorts
Individual Components of Endpoint

	Actively Monitored (per 100 person-years (95% CI)) N=1718	Observational Control (per 100 person-years (95% CI)) N=3371	Unadjusted Hazard Ratio (95% CI)	p-value	Adjusted* Hazard Ratio (95% CI)	p-value
Stroke	2.2 (1.8, 2.7)	2.6 (2.3, 3.0)	0.83 (0.65, 1.06)	0.13	0.79 (0.62, 1.01)	0.06
Myocardial Infarction	1.5 (1.2, 1.9)	1.8 (1.6, 2.2)	0.82 (0.62, 1.10)	0.19	0.82 (0.61, 1.10)	0.19
Systemic Emboli	0.84 (0.61, 1.2)	1.0 (0.8, 1.3)	0.80 (0.54, 1.18)	0.26	0.81 (0.55, 1.20)	0.29
Death	0.50 (0.33, 0.76)	0.81 (0.63, 1.0)	0.60 (0.37, 0.98)	0.04	0.61 (0.37, 0.99)	0.047
Stroke, MI, Emboli or death	4.5 (3.9, 5.2)	5.5 (5.0, 6.0)	0.81 (0.69, 0.96)	0.01	0.79 (0.66, 0.93)	<0.01

*Models adjust for the following baseline (pre-randomization date) covariates: age, female, Charlson Comorbidity Index, heart failure, COPD, chronic renal failure, diabetes, hypertension, obesity, stroke, prior myocardial infarction, sleep apnea, baseline ER visits, baseline PCP visits, and baseline hospitalizations.

Safety Endpoint - Entire Cohorts

	Actively Monitored (per 100 person-years (95% CI)) N=1718	Observational Control (per 100 person-years (95% CI)) N=3371	Unadjusted Incident Rate Ratio (95% CI)	p-value	Adjusted* Incident Rate Ratio (95% CI)	p-value
Total Hospitalizations	12.9 (11.9, 14.0)	18.9 (17.9, 19.8)	0.68 (0.62, 0.75)	<0.01	0.69 (0.63, 0.76)	<0.01
Hospitalizations for Bleeding	0.32 (0.19, 0.54)	0.71 (0.54, 0.92)	0.45 (0.25, 0.81)	<0.01	0.47 (0.26, 0.85)	0.01

*Models adjust for the following baseline (pre-randomization date) covariates: age, female, Charlson Comorbidity Index, heart failure, COPD, chronic renal failure, diabetes, hypertension, obesity, stroke, prior myocardial infarction, sleep apnea, baseline ER visits, baseline PCP visits, and baseline hospitalizations.

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Limitations

- The comparison between individuals choosing to participate in a randomized trial and an observational cohort may be biased by unmeasured confounding.
- Endpoints were based on claims data, limiting clinical follow-up to the duration of health plan enrollment, which was < 3 years for some participants.
- All treatment decisions were based on physician preference, and overall use of anticoagulants was low (<50%) in both cohorts.

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Conclusions

- Active screening for AF, as part of a prospective, pragmatic, direct-to-participant, nationwide study, was associated with a significant improvement in clinical outcomes and safety at 3 years relative to routine care.
- Independent replication of these findings is required in order to be confident that aggressive pursuit of diagnosing atrial fibrillation in people at high-risk, but without symptoms, is warranted.

Thank you to all of our mSToPS participants