WHERE MEDICAL DIRECTORS TRANSFORM KNOWLEDGE INTO IMPROVED OUTCOMES

Organization for Objective Review and Clinical Assessment (OORCA)

Objective Review and Clinical Assessment (ORCA)

for

Zio® XT

iRhythm Technologies

Commissioned by:

NAMCP Value-Based Care Council

April 25, 2023

WHERE MEDICAL DIRECTORS TRANSFORM KNOWLEDGE INTO IMPROVED OUTCOMES

Organization for Objective Review and Clinical Assessment (OORCA)

About NAMCP Medical Directors Institute

The National Association of Managed Care Physicians (NAMCP) Medical Directors Institute, a nonprofit membership association, was established in 1991 to provide tools, education, and resources to medical directors, practicing physicians, and other healthcare professionals. The membership consists of medical directors and physicians from purchaser, plan, and provider healthcare delivery systems. NAMCP offers educational materials, evidence-based tools, and resources to help Medical Directors from purchasers, plans, and provider systems make effective and informed decisions. NAMCP resources help members respond to opportunities and challenges while helping to improve healthcare outcomes, and ultimately the lives of members and patients.

About the Value-Based Care Council (VBCC)

In 2021, NAMCP established the Value-Based Care Council (VBCC) to address the changing landscape of healthcare delivery from traditional fee-for-service to value-based care. NAMCP recognized that pharmaceuticals are the mainstay of the treatment plan for most medical conditions, and the Association made the decision to move forward with an initiative to work with Medical Directors and other stakeholders to improve medical outcomes through more effective utilization of pharmaceuticals. The VBCC works with Medical Directors to develop solutions, including but not limited to standardized tools and resources, to assist in more effective extraction of pharmaceutical value so as to optimize medical outcomes. The Council is dedicated to assisting Medical Directors with achievement of the Triple AIM goals of improved outcomes, improved patient satisfaction, and reduced medical costs. The Council will focus on pharmaceutical value, adherence and persistency, strategies and methods to effectively leverage the value of pharmacy spend, and the critical components of pharmaceutical value-based contracts. In addition, the Council will explore and discuss other value-based care landscape issues and will engage in projects such as analytical studies and white papers that drive better informed policy, coverage, and healthcare delivery.

In response to an agreed upon unmet need in the marketplace, the VBCC developed a Short Form to enhance the effectiveness and efficiency with which product value propositions can be shared between industry and the medical leadership of various payers throughout the country. This Short Form allows concise and consistent sharing of product value propositions while enabling alignment of expectations before conversations or meetings regarding a product or service take place. The Short Form, which is intended to be utilized by the customer as an unsolicited request to industry, contains guidance for industry as it pertains to the customer and allows a response that does not exceed 3 pages in length.

About the Organization for Objective Review and Clinical Assessment (OORCA)

In 2022, the VBCC expanded its efforts beyond the Short Form by establishing the Organization for Objective Review and Clinical Assessment (OORCA), an independent third-party entity designed to conduct objective assessments of industry's product value propositions that are communicated to Medical Directors. Requests from payers, manufacturers, and others for an Objective Review and Clinical Assessment (ORCA) are received by the VBCC. The OORCA assesses credibility and objectivity of the manufacturer's value proposition of its product(s) based on available evidence for the following domains: 1) efficacy claims, 2) safety claims, 3) other patient outcomes or product attributes claims, and 4) economic claims. This assessment is intended to aid Medical Directors' evaluation of the product(s) for their organization and members.

Product Value Proposition Customer Engagement Short Form/Dossier

1. Drug/Product Name/Coordinated Solution

Zio® XT is a Food and Drug Administration (FDA)-cleared, single-use, noninvasive, water-resistant, long-term, continuous 14-day, ambulatory electrocardiogram (ECG) monitoring adhesive patch, also known as a medical magnetic tape recorder or a long-term continuous monitor (LTCM). The device captures and analyzes cardiac rhythms using the Zio ECG Utilization Service (ZEUS)—a software assistive augmented intelligence (AI) algorithm. Certified cardiac technicians (CCTs) complete the data analysis and generate the final Zio Report.

2. FDA Approved—Yes, No, or N/A

Zio XT received Section 510(k) clearance by the FDA in 2009.

Zio XT is indicated for use in patients who may be asymptomatic or who may suffer from transient symptoms such as palpitations, shortness of breath, dizziness, lightheadedness, presyncope, syncope, or anxiety.

3. Competitor Products or a Unique Entity

In general, other products designed for heart rhythm monitoring include:

- Holter monitors: provide continuous recording for 24 to 48 hours
- Event monitors: monitor for 2 to 4 weeks; record only arrhythmias via patient activation or automatic detection; some devices transfer data to a clinical staff center
- Mobile cardiac telemetry (MCT): this innovative event monitor provides real-time, attended cardiac monitoring; includes a sensor worn by the patient and a portable monitor with automated algorithms that trigger transmissions to a clinical surveillance center
- Implantable loop recorders: record for a prolonged period of time (up to 3 years); require a minimally invasive procedure; can be auto- or patient-triggered

4. Any Unique Technology, Delivery Mechanism, Solution Approach, or Therapeutic Advancement Integral to the Value Proposition

The Zio XT, also referred to as the Zio patch, is a long-term continuous ambulatory ECG heart monitor that is designed to be worn for up to 14 days. Advantages or benefits include:

- Long-term (up to 14 days) continuous monitoring can be provided
- Device is easily applied, lightweight, mobile, and water resistant
- Patch can be worn discreetly under garments, during sleep, while showering, and with moderate exercise
- Patient can press a button to capture symptomatic events

5. Professional Society/National Organization or Other Learned Body Recommendations

The American Heart Association, the American College of Cardiology, and the Heart Rhythm Society (AHA/ACC/HRS) recommend the use of ECG documentation to establish the diagnosis of atrial fibrillation (AF), for example, telemetry, Holter monitor, and event recorders. Prolonged or frequent monitoring may be necessary to reveal episodes of asymptomatic AF (January et al. 2014).

6. Included in Any Treatment Guidelines?

None applicable specifically to Zio XT.

7. Coding/Current Coverage

The Zio XT system is an extended continuous ambulatory cardiac monitor billed under procedure billing code CPT 93243 for greater than 48 hours and up to 7 days, or 93247 for greater than 7 days and up to 15 days. The following Billing and Coding information is provided by iRhythm:

- Application Component—billed by the ordering physician when Zio XT is applied on-site
  - CPT 93242, greater than 48 hours, and up to 7 days
  - CPT 93246, greater than 7 days, and up to 15 days
- Technical Component—billed by iRhythm
  - CPT 93243, greater than 48 hours, and up to 7 days
  - CPT 93247, greater than 7 days, and up to 15 days
- Interpretation—billed by interpreting physician
  - CPT 93244, greater than 48 hours, and up to 7 days
  - CPT 93248, greater than 7 days, and up to 15 days
- Global code for LTCM
  - CPT 93241, 3-7 days (inclusive of application, technical, and interpretation)
  - CPT 93245, 8-14 days (inclusive of application, technical, and interpretation)

8. Value Proposition

a) How Defined and Measured

The following information was obtained from iRhythm's Zio XT Clinical Value Dossier.

The Dossier summarizes 23 published studies (pages 33-37 and 58-80) and states the following about Zio XT:

- Produces better than 96% analyzable time out of total wear time
- Identifies multiple arrhythmia types with accuracy equivalent to that of a consensus panel of expert cardiologists
- Produces greater patient compliance than nonpatch alternatives
- Provides extended monitoring (beyond 48 hours), which is necessary to capture about one-third of arrhythmias
- Produces a diagnostic yield greater than shorter-term monitors and comparable with mobile telemetry and implantable monitors

- Can quantify burden of AF and other arrhythmias, likely producing a positive impact on patient health and clinical outcomes

Also described in the Dossier was analytic validity, or the ability of Zio XT to provide interpretable ECG data without significant variability. Analytic validity is stated to be greater than 96% analyzable wear time (Turakhia et al. 2013; Schreiber et al. 2014; Tung et al. 2015; Heckbert et al. 2018; Steinhubl et al. 2018; Wineinger et al. 2019).

Clinical validity, defined as the ability of a device to reliably distinguish between different arrhythmias, is accurate and is equivalent to that of a consensus panel of expert cardiologists (Turakhia et al. 2013; Solomon et al. 2016; Hannun et al. 2019).

Clinical utility of the Zio XT device relates to its ability to provide information that has a positive impact on patient management and/or treatment strategy. iRhythm states that the Zio XT offers the following clinical utilities:

- Monitoring for 7 to 14 days with a high-yield for arrhythmia identification (Rosenberg et al. 2013; Turakhia et al. 2013; Eisenberg et al. 2014; Tung et al. 2015; Turakhia et al. 2015; Solomon et al. 2016; Heckbert et al. 2018; Reed et al. 2018; Rooney et al. 2019; Schultz et al. 2019; Wineinger et al 2019)
- Greater diagnostic yield than is seen with alternative ambulatory cardiac monitors (Rosenberg et al. 2013; Barrett et al. 2014; Reynolds et al. 2023)
- Ability to impact patient management and treatment (Steinhubl et al. 2018; Schultz et al. 2019; Gladstone et al. 2021)
- High patient compliance (Turakhia et al. 2013; Tung et al. 2015; Chen et al. 2016; Solomon et al. 2016; Go et al. 2018; Heckbert et al. 2018; Reed et al. 2018; Hannun et al. 2019)
- Accelerated treatment by decreasing time to diagnosis (Reynolds et al. 2023)
- Enhanced patient experience (Barrett et al. 2014; Reed et al. 2018)
- Improved clinical outcomes such as reduced composite endpoint of death, stroke, systemic emboli, and myocardial infarction (Steinhubl et al. 2021)
- Reduced healthcare resource utilization and costs (Kaura et al 2019; Waalen et al. 2020; Reynolds et al. 2023)
- Lower likelihood of retesting (Reynolds et al. 2023)

An investigator-initiated randomized clinical trial (N=856) reported that screening with Zio XT significantly detected more AF in previously undiagnosed adults ≥75 years old with hypertension compared with standard clinical care and follow-up for 6 months, including pulse check and heart auscultation at baseline and at 6 months (5.3% vs 0.5%; relative risk, 11.2; 95% CI, 2.7-47.1, p=0.001) (Gladstone et al. 2021).

b) Medical Cost Offsets/Comparisons With Current Therapy/Burden of Disease Cost Reduction

The iRhythm Zio XT Clinical Value Dossier summarizes the economic impact of other cardiac monitoring devices such as ambulatory Holter monitors, mobile cardiac telemetry (MCT), external loop recorders, and implantable loop recorders (pages 49-51). The Dossier states that cost savings could be generated if use of the Zio XT reduced the need for repeated or prolonged Holter or event monitoring; however no direct evidence is presented in the Dossier to support this statement. The CAMELOT study described below shows that use of Zio XT resulted in less retesting compared with use of other monitors.

Although it is not included in the Dossier, iRhythm submitted the mHealth Screening to Prevent Strokes (mSToPS) trial, a randomized pragmatic trial that compared 1,718 older adults with no known AF and at

increased risk for stroke from a large health plan (Aetna Fully Insured Commercial and Medicare) versus 3,371 matched controls. The Zio XT patch was worn during the first 2 weeks and the last 2 weeks of a 4-month period. The actively monitored group incurred higher rates of cardiology visits, no differences in primary care visits, and lower rates of emergency department visits and hospitalizations (Waalen et al. 2020).

iRhythm submitted a poster presented at the American College of Cardiology conference in March 2023. CAMELOT is a large Medicare Fee-for-Service medical and pharmacy claims database study that analyzed healthcare resource utilization and costs associated with 4 ambulatory cardiac monitors: LTCM, Holter, external ambulatory event monitor (AEM), and mobile cardiac telemetry (MCT). Zio XT, an LTCM, was found to have the highest diagnostic yield, the lowest likelihood of retesting, and the lowest hospitalization utilization and total healthcare costs (Reynolds et al. 2023).

c) Value Based/Risk Offering?

iRhythm is currently developing risk-based contracts and will negotiate such contracts with provider groups and payers. Details are confidential at this time.

d) Response to ICER Report (if exists)

None applicable.

9. Landmark or Pivotal Clinical Study

Zio XT was cleared by the FDA via the Section 510(k) process, which determined that the device is substantially equivalent to legally marketed predicate devices in the market. Therefore, iRhythm was not required to conduct large, randomized, controlled trials. No landmark or pivotal clinical trials formed the basis for FDA clearance of Zio XT.

10. HEOR Support

a) Budget Impact Models/Predictive Modeling

iRhythm developed several models.

The Zio Atrial Fibrillation Model (Excel) is based on assumptions from the mSToPS trial (Steinhubl et al. 2018; Waalen et al. 2020). The baseline assumptions result in future cost savings from a health plan perspective. The model assumed lower rates of stroke, myocardial infarction (MI), systemic emboli, and death associated with Zio XT compared with a baseline scenario without Zio XT; however such assumptions are not rigorously supported by direct evidence for Zio XT.

The Zio Significant Yield Calculator (Excel) estimates the diagnostic rates of significant arrhythmias with various monitors (Zio XT, Holter, event monitor, MCT). The baseline assumptions compared Holter against Zio XT and predicted an additional 216 arrhythmias detected in a population of 1,000 patients eligible for monitoring. The reference used to support this model was Tsang et al. (2013).

The Zio Healthcare Resource Utilization Calculator (Excel) was developed to estimate healthcare resource utilization (HCRU) differences caused by diagnosing actionable arrhythmias in a US Commercial and Medicare Advantage health plan, based on assumptions from Steinhubl et al. (2018) and Tsang et al. (2013). The baseline model showed that at Year 1, inpatient, outpatient, and emergency department (ED) visits and costs are reduced with Zio XT compared with Holter.

The Zio Budget Impact Model (Excel) estimates the budget impact of Zio XT in a physician practice with an assumed 200 patients eligible for arrhythmia monitoring. Output costs include total monitoring costs, costs per treated patient, and costs related to improved management. References used to support this model include Barret et al. (2014), Tsang et al. (2013), and Arnold and Layton (2015).

b) Any RWE; Are There Patient/Clinical Registries?

iRhythm submitted the mHealth Screening to Prevent Strokes (mSToPS) trial, a randomized pragmatic trial that compared 1,718 older adults with no known AF and at increased risk for stroke from a large health plan (Aetna Fully Insured Commercial and Medicare) versus 3,371 matched controls. The Zio XT patch was worn during the first 2 weeks and the last 2 weeks of a 4-month period. The actively monitored group incurred higher rates of cardiology visits, no differences in primary care visits, and lower rates of ED visits and hospitalizations (Waalen et al. 2020).

iRhythm submitted a poster presented at the American College of Cardiology conference in March 2023. CAMELOT is a large Medicare Fee-for-Service medical and pharmacy claims database study that analyzed HCRU and costs associated with 4 ambulatory cardiac monitors: LTCM, Holter, AEM, and MCT. Zio XT, an LTCM, was found to have the highest diagnostic yield, the lowest likelihood of retesting, and the lowest hospitalization utilization and total healthcare costs (Reynolds et al. 2023).

Objective Review and Clinical Assessment of Manufacturer's Value Proposition

iRhythm's value proposition for the Zio XT cardiac monitor was assessed for credibility and objectivity based on available evidence submitted as of April 25, 2023.

Efficacy Claims

Although there are no traditional large, pivotal, label-enabling, Phase 3 trials that support the efficacy and FDA clearance of the Zio XT cardiac monitor, multiple studies published since 2013 have shown the clinical utility of the device to detect arrhythmias effectively, as outlined in #8a above. The value proposition for the Zio XT device is credible and objective based on available evidence as it relates to:

- Diagnostic yield, including compared with other alternatives (eg, Holter monitor)
- Analyzable wear time
- Detection of many types of arrhythmias
- Lower likelihood for retesting compared with other monitor types
- Improved clinical outcomes
- Decreased time to diagnosis

Safety Claims

No specific safety claims were made.

Other Claims About Patient Outcomes or Product Attributes

Patient compliance was shown in multiple studies to be high, as demonstrated by long median and mean wear times. Published studies have reported that patients preferred the Zio XT over the Holter monitor and found the device comfortable to wear (Barrett et al. 2014; Reed et al. 2018). Thus, claims about patient compliance and preference are credible and objective.

Economic Claims

The Dossier states that Zio XT reduces healthcare costs; however the only referenced study in the Dossier that supports cost savings is Kaura et al. (2019). Authors reported that an economic model demonstrated that Zio XT would result in more strokes avoided compared with Holter monitoring, which was associated with direct medical cost savings. Since the Dossier was developed, 2 additional studies have shown that Zio XT is associated with lower HCRU and costs (Waalen et al. 2020; Reynolds et al. 2023). Despite limited evidence for cost savings, iRhythm is the only manufacturer of cardiac monitors that have conducted and published real-world comparative economic and outcome data to support the value proposition of the Zio XT monitor. The economic claims for Zio XT are credible and objective. That said, additional research would be helpful to further elucidate the economic impact and cost-effectiveness of Zio XT compared to other modalities in monitoring and screening for arrhythmias.

Evidence Table for Zio® XT Studies Included in This Review

Citation Study Funding	Study Design Study Size	Patient Population	Intervention(s)	Outcome Measures	Wear Time	Results
Rosenberg et al. 2013 Funding: iRhythm	Single-center pilot study (appears prospective) N=74	Consecutive patients w/paroxysmal AF referred for Holter for arrhythmia detection 4/27/2011 to 5/25/2012 At Beth Israel Deaconess Medical Center, Boston, MA	Patients received both: Zio Patch (up to 14 d) + Holter monitor (24 hr)	• Determine pattern of AF • Document response to therapy • Potentially diagnose other arrhythmias	Mean wear time: • Zio 10.8 d (4-14 d)	• During first 24 hr, Zio Patch identified all AF episodes recorded by Holter • Mean AF burden in first 24 hr was 54.7% Zio vs 58.4% Holter (p<0.0001) • Total 454 patient-days were recorded by Zio where additional AF episodes were diagnosed in 43 (58.1%) patients; median time to detection was 1 d (range, 1-12 d) • Longer monitoring time with Zio detected significantly more patients (n=18) than were detected with Holter (p<0.0001) • AF burden in all patients with AF (n=43) on Zio was 28.4% • Classification of AF and management changed as a result of Zio in 21 patients; changes in antiarrhythmics (n=13) and anticoagulation (n=4); 2 received a pacemaker; 1 ablation; 1 pulmonary vein isolation procedure; 2 cardioversion • 49 patients discontinued study (16 device fell off; 6 decided to remove device; 1 battery malfunction; 1 unknown reason; 1 required cardiac intervention)

Turakhia et al. 2013
 	
Funding: iRhythm
	Cross-sectional database study
	
	N=26,751
		All patients who had Zio Patch monitoring for the first time
		
		1/1/2011 to 12/31/2011
		
		Using de-identified data from manufacturer
			Zio Patch	Evaluated:
				• Compliance (wear time)
				• Analyzable signal time
				• Interval to arrhythmia detection
				• Diagnostic yield
					Mean wear time:
					• 7.6 ± 3.6 d
						• Mean wear time was 7.6 d; median wear time was 7.0 d
						  ○ 95.6% wore >48 hr, 74.3% ≥6 d, and 16.1% ≥13 d
						• Median analyzable time was 99% of total wear time
						  ○ 87.1% had analyzable time ≥22 hr/d
						• Time to first arrhythmia was 1.7 d mean, 0.8 d median
						• Time to first symptom-triggered arrhythmia was 3.0 d mean and 2.9 d median
						• Among patients with arrhythmias, first arrhythmia occurred >48 hr from start of monitoring in 29.9%
						  ○ 71.1% were identified in first 2 d; 90% by 5th day
						• Among patients with symptom-triggered arrhythmias, 51.1% had first arrhythmia occur >48 hr from start of monitoring
						  ○ 46.2% were identified in first 2 d; 92% by 8th day

Barrett et al. 2014
 	
Funding: National Institutes of Health/National Center for Advancing Translational Sciences and iRhythm
	Prospective study in clinic
	
	N=146
		Patients referred for arrhythmia evaluation
		
		April 2012 to July 2012
		
		At Scripps Green Hospital, La Jolla, CA
			Patients received both:
			
			Zio Patch
			+
			24-Hour Holter monitor
				Primary:
				• Compare arrhythmia detection over total wear time of both devices
				
				Secondary:
				• Compare arrhythmia detection over simultaneous initial 24-hr period
				• Survey patient preferences
					Median wear time:
					• Zio 11.1 d (0.9-14.0 d)
					• Holter 1.0 d (0.9-1.0 d)
						• Zio detected significantly more events than were detected by Holter (96 vs 61; p<0.001) over total wear time
						  ○ 60 events were detected by both
						  ○ 36 events were undetected by Holter
						  ○ 1 event was detected by Holter but not by Zio
						• Holter detected significantly more events than Zio (61 vs 52; p=0.13) over simultaneous 24-hr period
						  ○ 50 events were detected by both
						  ○ 11 events were undetected by Zio
						  ○ 2 events were detected by Zio but not by Holter
						  ○ 10 of 11 events were undetected by Zio later detected by Zio
						• 93.7% (134/143) found Zio comfortable vs 51.7% (74/143)
						• Zio affected 10.5% (15/143) of activities of daily living vs 76.2% (109/143) for Holter
						• 81% (111/137) preferred Zio over Holter monitor
						• 90% (92/102) of surveyed physicians thought definitive diagnosis was achieved using Zio vs Holter 64% (65/102)

Citation Study Funding	Study Design Study Size	Patient Population	Intervention(s)	Outcome Measures	Wear Time	Results
Eisenberg et al. 2014 Funding: none	Cross-sectional study N=524	Consecutive patients referred to a single-center, 5-physician, academic ambulatory electrophysiology practice and prescribed Zio Patch 5/28/2010 to 1/11/2013	Zio Patch	• Indications for use • Diagnostic yield	Mean wear time: • 7 d (0.33-14 d)	• Indications: unspecified arrhythmias or palpitations (47%), known or suspected AF (30%), syncope (8%), bradycardia surveillance (4%), tachyarrhythmia surveillance (5%), chest pain (2%) • Arrhythmia was detected in 99.5% of patients • 297 (57%) had significant arrhythmias; mean 2.7 episodes/patient • Most (66%) had first event within 48 hr and 34% continued to accumulate unique arrhythmia out to 12 d • 105 (20%) were identified with AF, of whom 49 (47%) had paroxysmal AF • Mean monitoring period required to detect AF was 67 hr (2.8 d) • Patient-triggered events were recorded in 310 (59%) patients, with most patients (79%) triggering the event button more than once (range, 1-298)
Schreiber et al. 2014 Technical support: iRhythm	Observational study N=174	Convenience sample of discharged adult ED patients with symptoms of possible arrhythmia deemed candidates for outpatient ambulatory cardiac monitoring Feb 2011 to Feb 2012 At 3 academic EDs in US	Zio Patch	• Determine diagnostic yield • Determine value of prolonged monitoring of low-risk discharged ED patients with possible arrhythmia	Median wear time: • 6.9 d (IQR 5.8-9.2 d)	• Diagnostic yield was 63.2%—calculated to be the number of triggered events without arrhythmias (n=93) and the number of significant symptomatic arrhythmias detected (n=17) • Analyzable time was 98.6% of total recorded data • 83 patients (47.7%) had ≥1 significant arrhythmia (excluding chronic atrial fibrillation) and 17 (9.8%) were symptomatic at the time of their arrhythmia • 9 patients (5.2%) had ≥2 arrhythmias • Median time to first arrhythmia was 1.0 d and median time to first symptomatic arrhythmia was 1.5 d • 93 (53.4%) symptomatic patients did not have any arrhythmias during their triggered events
Camm et al. 2015 Funding: Medtronic	Registry analysis N=40	Patients from arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) registry 4/18/2013 to 5/23/2013 At Johns Hopkins, Baltimore, MD	Zio Patch for 7 d	• Examine variability of PVC counts in sequential 24-hr periods using 7-d monitoring devices	Mean wear time: • 159 ± 39 hr	• Median 24-hr PVC count was 1,090.5 (IQR 1,711) • Substantial day-to-day variability of PVC frequency ranged from 31% to 2,709% compared with the patient's median 24-hr PVC count • Difference between max and min PVC count was highly variable in 76% of participants
Tung et al. 2015 Funding: not stated	Database study N=1,171	Patients with Zio for TIA or stroke Jan 2012 to June 2013 Obtained de-identified monitoring data from iRhythm	Zio Patch	• Duration of monitoring • Analyzable signal time • Numbers and types of arrhythmia • Time to first arrhythmia	Median wear time: • 13.0 d (IQR 7.2-14.0 d)	• 97.1% wore ≥48 hr, 91.9% ≥4 d, and 66.9% ≥10 d • Mean analyzable time was 95.8%; median was 98.7% • Frequency of AF was 5% at 14 d (4.4% PAF and 0.6% chronic AF) • Mean duration before first PAF was 1.5 d; median duration was 0.4 d • 14.3% of first PAF episodes occurred after 48 hr • Mean PAF burden was 12.7% of total monitoring duration • Mean duration before first SVT was 2.1 d

Citation Study Funding	Study Design Study Size	Patient Population	Intervention(s)	Outcome Measures	Wear Time	Results
Turakhia et al. 2015 In-kind support by iRhythm in form of extended ambulatory monitors	Single-center, single-arm, prospective screening study N=75	Age ≥55 y and ≥2 risk factors: CAD, CHF, HTN, DM, sleep apnea Excluded prior AF, stroke, TIA, and implantable pacemaker or defibrillator, or with palpitations or syncope in the prior year May 2012 to August 2013	Zio Patch	Primary: • Presence of AF by Zio Secondary: • SVT, VT, and SVE	Median wear time: • 13 d (7.8-14 d) Mean wear time: • 10.4 ± 4.5 d	• AF was detected in 4 (5.3%) patients with mean AF burden 28% ± 48% • Any arrhythmia of ≥8 consecutive beats detected in 36 (48%) patients • 18 (24%) patients had no arrhythmias • All episodes of SVT were AT and were present in 67% (≥4 beats), 44% (≥8 beats), and 6.7% (≥60 s) of patients • SVE was detected in 74 (99%) patients without sustained AT/AF • No sustained VT was detected
Chen et al 2016 Supported by National Heart, Lung, and Blood Institute	Cross-sectional study N=325	Participants in Atherosclerosis Risk in Communities (ARIC) study July 2013 to Mar 2014	None	• Association between AF burden and cognitive function	Median wear time: • 13.9 d (13.3-14.0 d)	• Noted Zio "performed very well" and reported median wear time and analyzable time • However, study was not focused on investigating Zio patch; rather it was conducted to elucidate AF burden with cognition
Loring et al. 2016 No financial disclosures	Database study N=101	Patients with PVC >1.0% of heartbeats Mar 2012 to Mar 2015 At San Francisco VA in California	Zio Patch	Evaluated: • PVC counts		• Median analyzable time was 11.6 d (IQR, 10.8-13.8 d) • Median PVC burden was 2.6% of total heartbeats • Clinically significant PVC thresholds were defined as 10%, 15%, or 20% of total heartbeats. Among patients who crossed thresholds, only 6.9%, 4.0%, and 1.0% reached their maximum PVC burden in the first 48 hr • Median time to cross thresholds: 1 d for 10% and 20% thresholds; 2 d for 15% threshold • On first day, 75% of people crossed the 20% threshold; 53% crossed the 10% threshold; 47% crossed the 15% threshold
Soloman et al. 2016 Funding: iRhythm	Data analysis N=122,815 records contributed by 122,454 patients	All data for Zio Service long-term continuous ambulatory ECG monitors Nov 2011 to Dec 2013 Analysis of de-identified dataset provided by iRhythm	Zio Patch XT	• Measure burden and timing of high-risk arrhythmias	Mean wear time: • 9.6 + 4.0 d Median wear time: • 9.9 d (IQR 6.8-13.8 d)	• 22,443 (18%) had nonsustained VT; 238 (0.2%) sustained VT; 1,766 (1.4%) sinus pause >3 s; 521 (0.4%) AF pause >5 s; 249 (0.2%) symptomatic pause; 1,468 (0.4%) high-grade heart block • For sustained VT, only 52.5% of total identified arrhythmias were identified at 24 hr and 65.5% were identified by 48 hr • Most arrhythmias were identified by 7 d (92.9%) • Monitoring between 7 and 14 d yielded additional 7.1% • For most common bradyarrhythmia, sinus pauses were >3 s (N= 1,766); 31.7 % of total detected arrhythmias were found within 1 d, 46.6% within 2 d, and 83.1% within 3 d of monitoring
Go et al. 2018 Funding: iRhythm	Retrospective cohort study N=1,965	Kaiser patients N. CA and S. CA w/ paroxysmal AF on Zio Oct 2011 to Oct 2016	None	• Hospitalization for ischemic stroke or arterial thromboembolism while not taking anticoagulants	Median wear time: • 14 d (11-14 d)	• Study objective was to determine burden of AF and risk of ischemic stroke or thromboembolism • However, study was not focused on investigating Zio patch

Citation Study Funding	Study Design Study Size	Patient Population	Intervention(s)	Outcome Measures	Wear Time	Results
Heckbert et al. 2018 Funding: National Heart, Lung, and Blood Institute	Epidemiologic study N=1,122 N=580 wore 2 devices	Patients of general population from Multi-Ethnic Study of Atherosclerosis 9/6/16 to 10/12/17	Zio Patch XT × 1 vs Zio Patch XT × 2	Outcomes: • Acceptability of patch ECG monitor • Yield of arrhythmia detection • Consistency of findings in participants monitored twice	Median wear time: • 14.0 d (13.2-14.0 d)	• Median analyzable time: 13.8 d (12.8-14.0 d) • 4% reported skin irritation • In Analysis 1, AF or atrial flutter was detected in 7.3% (69/946) during the 12 d of monitoring • Among participants with no prior clinical history of AF/flutter and at least 12 d of monitoring on a single device, AF/flutter was detected in 32/804 (4.0%) ○ 38% of these were first detected from Days 3-12 • Among participants with a history of clinically recognized AF/flutter, 26% had AF/flutter and 74% had no AF/flutter detected during 12 d of monitoring • 439/580 with 2 devices had data showing excellent agreement for supraventricular and ventricular ectopic beats per hour, fair agreement for high-grade atrioventricular block, and pauses of greater than 3 seconds' duration
Muse et al. 2018 Funding: National Institute of Health; Quest Diagnostics	Prospective multicenter study N=904	≥40 yo 1 risk factor for AF, with symptoms AF, or first diagnosis AF 12/2/2013 to 01/19/2016	Zio Patch vs Long-term Holter And AF genetic testing	Primary event was AF/atrial flutter Validate AF GRS for identifying patients at increased risk for AF	Mean wear time: 10 d 21 hr (Zio) vs 13 d 18 hr (Holter)	• AF was discovered in 44 patients (Zio) and in 42 patients (Holter) • Highest AF GRSs were 3× more likely to be diagnosed with AF than with low GRS
Reed et al. 2018 Funded: Chest, Heart, and Stroke Scotland iRhythm technologies provided Zio Patch and ECG analysis	Prospective pilot study N=86	≥16 yo presenting to ED within 6 hr of syncope 11/17/15 to 6/16/17 At ED in UK tertiary center	Zio Patch XT vs Historical unmatched comparator group (n=603 from ROSE study)	Primary endpoints: • Symptomatic significant arrhythmia at 90 d f/u • Diagnostic utility Secondary endpoints: • Median time to detection • Prevalence in 90 d f/u • Satisfaction • Compliance • Referrals and/or cardiac investigation • All-cause serious outcomes at 90 d	Median wear time: • 13.6 d (11.8-14.0 d)	• 90-Day diagnostic yield for symptomatic significant arrhythmia ○ 10.5% (9/86) vs 2.0% (12/603) in comparator • 56/76 (73.7%) with returned Zio had diagnostic finding ○ 34/56 (61%) had symptomatic sinus rhythm or ectopic beats only • Median time to symptomatic significant arrhythmia was 19 d (IQR 4-30; n=9) for Zio vs 8 d (IQR 5-17; n=12) in the comparator group • 24 patients had significant arrhythmia detected by 90 d • 43/47 (91%) agreed or strongly agreed that Zio was easy to use; 34/47 (72%) comfortable to wear; 39/47 (82%) able to carry out normal activities; 38/47 (80%) would use the patch monitor if required in the future • Patch irritated the skin 6/47 (13%); lost adherence to skin 7/47 (15%) • After ED assessment, no patients were referred to ECG service; by 90 d, 12 patients were referred • Per blinded cardiologists, Zio would significantly reduce need for standard OP ambulatory ECG from 84% to 1% (Expert 1) and from 81% to 8% (Expert 2) • Nonsignificant increase was seen in OP echocardiograms from 28% to 49% (Expert 1) and from 15% to 18% (Expert 2), and nonsignificant no further cardiac investigation was noted from 11% to 29% (Expert 1) and from 14% to 77% (Expert 2)

Citation Study Funding	Study Design Study Size	Patient Population	Intervention(s)	Outcome Measures	Wear Time	Results
Rho et al. 2018 MD initiated study supported by BDx	Prospective comparative N=29	Patients referred to a community cardiology practice	Zio Patch XT vs Carnation Ambulatory Monitoring (CAM) For 7 d	Primary endpoint: • Differences in rhythm types diagnosed between the 2 monitors Secondary endpoints: • Variances in findings resulting in differences in clinical decision making • Ease of use and comfort of each monitor		• 86.7 ± 0.6 arrhythmias were seen from Zio and 121.7 ± 2.1 from CAM (p<0.001) • Atrial tachycardia was diagnosed by CAM 22.3 ± 0.6 vs Zio 8.7 ± 3.2 (p<0.001) • Atrial flutter was diagnosed on CAM 3 ± 0 vs Zio XT 0.67 ± 0.58 (p<0.002) • CAM reports were able to assign a specific rhythm diagnosis beyond "SVT unknown" vs unable to assign a specific rhythm diagnosis for "SVT unknown" for ≥1 ECG strip on 15.7 ± 2.2 Zio XT reports • Diagnosis of NSVT was seen. In 4.7 ± 0.6 Zio reports vs 11.7 ± 1.5 CAM (p<0.001) • ECG clarity was ranked as high in all 29 CAMs (100%) vs 4.5 (16%) Zio (p<0.001) • CAM was slightly easier to attach and remove, was more stable, and was associated with less skin reaction; patient experiences were comparable and favorable for both
Steinhubl et al. 2018 Funding: Janssen, Scripps Research Translational Sciences, and Qualcomm Foundation mSToPS Trial	Direct-to-participant pragmatic RCT N=359,161 Prospective matched observational cohort study (Aetna Commercial and Medicare Advantage claims)	Aetna Fully Insured Commercial and Medicare populations. ≥75 years, male >55 years, female >65 years w/ 1 or more prespecified comorbidities	Active home-based monitor for up to 4 wk (n=2,659) • Immediate within 2 weeks (n=1,366) • Delayed for 4 months later (n=1,293) 481 wore 1 patch 1,257 wore both patches vs Observational matched cohort (n=3,476)	Primary endpoint: • Incidence of newly diagnosed AF at 4 mo Secondary endpoints: • New AF at 1 y • Clinical consequences associated with ECG screening	Mean: 11.7 (4.1) d with 97.8% analyzable ECG data 481 individuals wore 1 patch 1,257 wore both ECG patches	• ITT new AF was 3.9% (53/1,366) immediate group and 0.9% (12/1,293) delayed • Per-protocol (only those who wore patch) was 5.1% (46/906) vs 0.6% (5/832) • In observational study, new AF was detected in 109/1,738 (6.7 per 100 person-years) in actively monitored cohort and in 81/3,476 (2.6 per 100 person-years) among observational controls • 65 actively monitored individuals were first to have AF by ECG patch; 43 with 1st patch and 22 only with 2nd patch • Active monitoring was associated with a higher rate of initiation of anticoagulant therapy (5.7 vs 3.7 per 100 person-years) • 40 individuals reported skin irritation, 32 discontinued early, 2 sought medical attention and received topical therapy
Wineinger et al. 2019 Supported by: NIH/NCATS Clinical and Translation Service Award	Retrospective analysis of longitudinal data N=13,293 records	Patients with PAF referred for extended rhythm evaluation Nov 2014 to Sept 2016 Data from iRhythm Inc. database Excluded: no PAF episodes, persistent AF	Zio Patch	Evaluated: • Frequency • Duration • Timing of event	Mean wear time: • 11.4 d	• Mean analyzable time was 11.1 d • Median daily rate of PAF events was 1.21 (IQR, 0.31-4.99) • 13.0% averaged 1 PAF event every 2 hr • 6.5% averaged ≥1 event each hour • 1,791 (13.5%) experienced a single event during full study • Average duration was 16.6 min, with median of 2.0 min (IQR, 54 s-6.7 min) • Median time to 1st detected PAF event was 24.9 hr (IQR, 2.7-83.9 hr) • After 24 hr of monitoring, 49.4% with PAF experienced a PAF event; increased to 63.1% after 48 hr; 89.7% after extended monitoring to 7 d

Citation Study Funding	Study Design Study Size	Patient Population	Intervention(s)	Outcome Measures	Wear Time	Results
Schultz et al 2019 Funding: None	Single-center retrospective cohort study N=314	Adults with congenital heart disease (ACHD) who underwent extended continuous ambulatory rhythm monitors (ECAM) June 2013 to May 2016 Raw data obtained from iRhythm	Zio Patch XT	Primary endpoint: • Time to first arrhythmia detected on continuous monitoring, whether prior to or after 48 hr Secondary endpoint: • Whether management changes were made based on arrhythmias detected on ECAM	Mean wear time: • 9.5 ± 4.1 d	• 72/156 (46%) with significant arrhythmias were noted within 48 hr • Arrhythmia incidence increased with time: 15% at 1 d, 23% at 2 d, 39% at 5 d, 47% at 7 d, 52% at 10 d, and 62% at 14 d • Symptomatic arrhythmia continued to increase: 12% at 1 d, 18% at 2 d, 36% at 5 d, 43% at 7 d, 50% at 10 d, and 61% at 14 d • 19% of monitors ordered for symptoms resulted in a care change • 15% of screening monitors resulted in a care change • 17% of monitors ordered for other abnormal testing resulted in a care change. • 16% of patients with any arrhythmia had a care change (49 patients) ○ 57% had care change for arrhythmia noted within 48 hr ○ 43% had care change for arrhythmia noted after 48 hr
Hannun et al 2019 Funding: iRhythm	Retrospective validation study N=53,877	De-identified data from adult patients ≥18 who used a single-lead ambulatory ECG monitor device (Zio Monitor) Jan 2013 to Mar 2017	None	• Performance of DNN against gold standard cardiologist consensus committee diagnoses obtained by calculating AUC	Mean wear time: • 10.6 d Median wear time: • 13.0 d	• Study objective was to develop a DNN to classify rhythms using Zio • However, study was not focused on investigating Zio patch
Kaura et al. 2019 Funding: Bristol-Myers-Squibb	Prospective open-label randomized controlled trial N=116	Adults with stroke or TIA within past 72 hr Feb 2016 to Feb 2017	Zio Patch XT (n=56); also got Holter vs Holter (n=60)	Primary outcome: • ≥1 PAF lasting 30 s within 90 d Secondary outcomes: • PAF within 28 d • PAF within 90 d in patients who got both • Ischemic stroke or TIA and mortality at D 90	Mean wear time: ZioPatch: 283.8 + 88.7 hr 96.4% completed 14 d Holter: 25.0 ± 25.0 hr	• Mean time from stroke/TIA to device placement was 2.1 ± 1.2 d with Zio and 38.9 ± 33.6 d with Holter • Rate of detection of PAF at 90 d: 16.3% for Zio and 2.1% for Holter, OR 8.9 (95% CI, 1.1-76.0; p=0.026); "Zio was superior to Holter" • Rate of detection of PAF at 28 d ○ 14.0% (6) Zio vs 2.1% (1) Holter (OR 7.5; 95% CI, 0.9-64.7; p=0.05) • Detection of PAF at 90 d in patients with Zio + Holter ○ 16.3% (7) Zio vs 4.7% (2) Holter (OR 4.0; 95% CI, 0.8-20.4; p=0.16) • No difference was noted in rate of recurrent ischemic stroke or TIA or mortality • An economic model demonstrated that Zio would result in 10.8 more strokes avoided per year compared with Holter monitoring, with an associated yearly savings in direct medical costs of £113,630, increasing to £162,491 over 5 y
Rooney et al. 2019 Funding: NHLBI, NIH, DHHS, AHA	Cross-sectional analysis study	Participants from the community-based multi-center observation ARIC study (Atherosclerosis Risk in Communities) N=2,616 2016 to 2017	Zio 2 wk vs Zio twice for 4 wk (n=386)	Prevalence of subclinical AF	Mean: 13.3 ± 1.7 d for first Zio XT patch, 13.1 ± 2.0 for second patch. 26.4 ± 2.9 for combined 4 wk	• Monitoring beyond 2 wk provided substantial incremental diagnostic yield • Median duration continuous analyzable time was 13.7 d (25th percentile, 12.7; 75th percentile 13.9; range, 0.1-14.0) • AF was detected in 217/2,616 (8.3%) participants ○ 87 (40.0%) intermittent AF, 130 (60.0%) continuous AF • Prevalence of subclinical AF was 2.5%—lower than was previously reported

Citation Study Funding	Study Design Study Size	Patient Population	Intervention(s)	Outcome Measures	Wear Time	Results
Eysenck et al. 2020 Funding: iRhythm, NUUBO Smart Solutions Technology, Bardy Diagnostics	RCT	Patients with permanent pacemakers (PPMs) and h/o AF UK study N=21	Zio XT vs NUUBO vest vs CAM vs Novacor "R" test 4 (RT) commonly used ECM Wore all 3 novel ECMs + RT in random order	Primary analysis: • Total AF burden Secondary analysis: • Individual episodes of AF • Likelihood of disagreement between ECM and PPM	Mean wear time: • 307 hr (Zio) vs 223 hr (RT) (p=0.016) • No diff between NUUBO or CAM vs RT	• All ECM devices significantly better estimated AF burden vs RT (p<0.0001) using DDDRP PPM as comparator • Zio and CAM more accurately indicated presence or absence of AF than RT • CAM caused significantly less discomfort than RT during initial application; so significant difference was noted between other ECMs and RT
Waalen et al. 2020 Funding: Janssen Pharmaceuticals, Scripps Research Translational Sciences, and Qualcomm Foundation mSToPS trial	Siteless, pragmatic trial conducted among large health insurance plan's members throughout the US	Aetna Fully Insured Commercial and Medicare populations, ≥75 y, male >55 y, female >65 y w/ 1 or more prespecified comorbidities 1,718 actively monitored 3,371 matched controls Utilization data from insurer's claim databases	Actively monitored with Zio Zio Patch first 2 wk vs Zio Patch last 2 wk 4-Month monitoring period	• Compare HCRU during year following screening for AF by patch vs matched cohort		• Diagnosis of AF by patch or clinical diagnosis after 1 y following initiation of patch wear was significantly higher among actively monitored • 41/65 (63.1%) actively monitored participants with AF detected on at least 1 patch received clinical diagnosis of AF during the year • 24/114 (21%) in actively monitored cohort with new AF diagnosis were not clinically diagnosed by their provider(s) as having AF • Median AF burden in those w/clinical diagnosis vs w/o: 1.5% vs 0.1% (p=0.004) • 30/77 (39.0%) actively monitored with AF were prescribed anticoagulation • Actively monitored group had significantly higher rates of cardiology visits, no differences in primary care visits, and lower rates of ED visits and hospitalizations compared with controls • Among those with newly diagnosed AF, reduction in ED visits and in hospitalizations was even greater (0.27 [0.17, 0.43])
Gladstone et al. 2021 Funding: C-SPIN; German Centre for Cardiovascular Research; Boehringer Ingelheim; Microlife Corp, ManthaMed, and iRhythm	Investigator-initiated, multicenter, randomized clinical trial N=856	≥75 yo with hypertension and without known AF in Canada and Germany Apr 2015 to Mar 2019	Zio for 2 wk at baseline and at 3 mo (n=434) vs Standard of care—routine clinical f/u pulse check and heart auscultation at baseline and at 6 mo (n=422)	Primary outcome: AF detected by ECG or clinical within 6 mo Secondary outcomes: Anticoagulant use Device adherence AF detection by BP monitors	Median: 27.5 of 28 d 14.0 d for 1st monitor 13.9 d for 2nd monitor	• 423 (97.5%) wore first monitor; 344 (79.3%) wore second monitor • 93.8% completed at least 1 wk of monitoring; 85.9% 2 wk, 74.2% 3 wk • Median analyzable time was 13.7 d and 13.5 d for 1st and 2nd monitoring, with 26.8 d total • AF at 6 mo occurred in 24/434 (5.3%) in Zio group vs 2/422 (0.5%) in control group (relative risk, 11.2; 95% CI, 2.7-47.1; p=0.001; absolute difference, 4.8%; 95% CI, 2.6%-70%; p<0.001) • In Zio group, 20/23 (87.0%) AF cases were detected by monitor and 3/23 (13.0%) were diagnosed clinically (hospitalized with symptomatic ECG documents AF) • Oral anticoagulant use was 4.1% vs 0.9% at 6 mo

Citation Study Funding	Study Design Study Size	Patient Population	Intervention(s)	Outcome Measures	Wear Time	Results
Steinhubl et al. 2021 Funding: Janssen, Scripps Research Translational Sciences, and Qualcomm Foundation mSToPS Trial	Direct-to-participant, pragmatic RCT N=359,161 Prospective matched observational cohort study (Aetna Commercial and Medicare Advantage claims)	Aetna Fully Insured Commercial and Medicare populations. ≥75 years, male >55 years, female >65 years w/ 1 or more prespecified comorbidities	Active home-based monitor for up to 4 wk (n=2,659) • Immediate within 2 weeks (n=1,366) • Delayed for 4 months later (n=1,293) 481 wore 1 patch 1,257 wore both patches vs Observational matched cohort (n=3,476)	Prespecified outcome: • At 3 years, time to first event of the combined endpoint of stroke, systemic embolism, or MI with and without death Primary safety endpoint: • Incidence of hospitalizations with primary diagnosis of bleeding Prespecified outcomes at 3 years after initiation of ECG screening • Time to first event of combined endpoint of stroke, systemic embolism, or MI, and with or without death		• Mean follow-up was 29 months • At end of 3 years, AF was newly diagnosed in 11.4% of those actively monitored vs 7.7% in observational group (p<0.01) • Rate of combined endpoint of death, stroke, systemic emboli, and MI was 3.6 per 100 person-years (95% CI 3.1-5.1) in actively monitored group and 4.5% (95% CI 4.0-5.0) in observational group (adjusted HR 0.79, p=0.02) • The combined endpoint, excluding death, was also significantly lower (3.3 vs 4.0 per 100 person-years), as were the individual endpoints of mortality (0.50 vs 0.81 per 100 person-years) and stroke (1.7 vs 2.2 per 100 person-years) • Rates of hospitalization for bleeding were 0.32 per 100 person-years in the actively monitored cohort vs 0.71 per 100 person-years in the control group with an adjusted incidence rate ratio of 0.47, p<0.01
Reynolds et al. 2023 CAMELOT study Funding: iRhythm	Retrospective cohort analysis of Medicare Fee-for-Service claims	Patients ≥65 yo assigned with an ACM for the first time and with no prior diagnosis of arrhythmia during the period Jan 1, 2017, through Dec 31, 2018 Jan 1, 2016, through Dec 31, 2019	LTCM (>48 hr to 14 d) including Zio XT vs Holter (≤48 hr) vs External AEM (noncontinuous up to 30 d) vs MCT (direct cell transmission up to 30 d)	Primary outcome: Compare occurrence and time-to-event (TEE) of CV events, CV procedures, and death Secondary outcomes: • Difference in ACM retest rates and diagnostic yield • Direct healthcare resource utilization and healthcare costs		• Diagnostic yield within 90 d was highest for LTCM (33.8%), followed by MCT (27.1%), external AEM (24.6%), and Holter (22.7%) • Zio XT subgroup of LTCM had the highest 90-d diagnostic yield (35.2%) • Retesting rate within 6 mo was lowest for Zio XT (16.8%); Holter (21.2%), LTCM (21.4%), MCT (36.2%), external AEM (46.6%) • All-cause hospitalizations were lowest with LTCM and Holter • All-cause ED visits were least common with LTCM • Outpatient visits were lowest in Holter and external AEM • Holter, external AEM, and MCT had higher hospitalizations, ED visits, and outpatient visits than LTCM • Zio XT was independently associated with highest diagnostic yield, lowest risk for repeat ACM testing, and lowest acute care hospitalization

ACHD=adult with congenital heart disease; ACM=arrhythmogenic cardiomyopathy; AEM=external ambulatory event monitor; AF=atrial fibrillation; AHA=American Heart Association; AT=atrial tachycardia; AUC=area under the curve; BP=blood pressure; CAD=coronary artery disease; CAM=Carnation Ambulatory Monitoring; CHF=congestive heart failure; CV=cardiovascular; DHHS=US Department of Health and Human Services; DM=diabetes mellitus; DNN=deep neural network; ECAM=extended continuous ambulatory monitor; ECG=electrocardiogram; ECM=external cardiac monitor; ED=emergency department; GRS=genetic risk factors; HCRU=healthcare resource utilization; HR=hazard ratio; HTN=hypertension; IQR=interquartile ratio; ITT=intent-to-treat; LTCM=long-term continuous monitor; MCT=mobile cardiac telemetry; NIH/NCATS=National Institutes of Health/National Center for Advancing Translational Science; NHLBI=National Heart, Lung, and Blood Institute; NSVT=nonsustained ventricular tachycardia; OP=outpatient; OR=odds ratio; PAF=paroxysmal atrial fibrillation; PPM=permanent pacemaker; PVC=premature ventricular contraction; RCT=randomized controlled trial; RT=Novacor "R" Test 4; SVE=supraventricular ectopy; SVT=supraventricular tachycardia; TEE=time-to-event; TIA=transient ischemic attack; VT=ventricular tachycardia

Publications Cited:

1. Arnold R, Layton A. Cost analysis and clinical outcomes of ambulatory care monitoring in Medicare patients: describing the diagnostic odyssey. JHEOR. 2015;2(2):161-169. doi: 10.36469/9897

2. Barrett PM, Komatireddy R, Haaser S, et al. Comparison of 24-hour Holter monitoring with 14-day novel adhesive patch electrocardiographic monitoring. Am J Med. 2014;127(1):95 e11-7. doi: 10.1016/j.amjmed.2013.10.003

3. Camm CF, Tichnell C, James CA, et al. Premature ventricular contraction variability in arrhythmogenic right ventricular dysplasia/cardiomyopathy. J Cardiovasc Electrophysiol. 2015;26(1):53-7. doi: 10.1111/jce.12544

4. Chen LY, Agarwal SK, Norby FL, et al. Persistent but not Paroxysmal Atrial Fibrillation Is Independently Associated With Lower Cognitive Function: ARIC Study. J Am Coll Cardiol. 2016;67(11):1379-80. doi: 10.1016/j.jacc.2015.11.064

5. Eisenberg E, Carlson S, Doshi R, Shinbane J, Chang P, Saxon L. Chronic ambulatory monitoring: results of a large single-center experience. J innov Card Rhythm Manag. 2014(November):1818-1823. doi: 10.19102/icrm.2014.051105

6. Eysenck W, Freemantle N, Sulke N. A randomized trial evaluating the accuracy of AF detection by four external ambulatory ECG monitors compared to permanent pacemaker AF detection. J Interv Card Electrophysiol. 2020;57(3):361-369. doi: 10.1007/s10840-019-00515-0

7. Gladstone DJ, Wachter R, Schmalstieg-Bahr K, et al. Screening for Atrial Fibrillation in the Older Population: A Randomized Clinical Trial. JAMA Cardiol. 2021;6(5):558-567. doi: 10.1001/jamacardio.2021.0038

8. Go AS, Reynolds K, Yang J, et al. Association of Burden of Atrial Fibrillation With Risk of Ischemic Stroke in Adults With Paroxysmal Atrial Fibrillation: The KP-RHYTHM Study. JAMA Cardiol. 2018;3(7):601-608. doi: 10.1001/jamacardio.2018.1176

9. Hannun AY, Rajpurkar P, Haghpanahi M, et al. Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network. Nat Med. 2019;25(1):65-69. doi: 10.1038/s41591-018-0268-3

10. Heckbert SR, Austin TR, Jensen PN, et al. Yield and consistency of arrhythmia detection with patch electrocardiographic monitoring: The Multi-Ethnic Study of Atherosclerosis. J Electrocardiol. 2018;51(6):997-1002. doi: 10.1016/j.jelectrocard.2018.07.027

11. Kaura A, Sztriha L, Chan FK, et al. Early prolonged ambulatory cardiac monitoring in stroke (EPACS): an open-label randomised controlled trial. Eur J Med Res. 2019;24(1):25. doi: 10.1186/s40001-019-0383-8

12. Loring Z, Hanna P, Pellegrini CN. Longer Ambulatory ECG Monitoring Increases Identification of Clinically Significant Ectopy. Pacing Clin Electrophysiol. 2016;39(6):592-7. doi: 10.1111/pace.12852

13. Muse ED, Wineinger NE, Spencer EG, et al. Validation of a genetic risk score for atrial fibrillation: A prospective multicenter cohort study. PLoS Med. 2018;15(3):e1002525. doi: 10.1371/journal.pmed.1002525

14. Reed MJ, Grubb NR, Lang CC, et al. Diagnostic yield of an ambulatory patch monitor in patients with unexplained syncope after initial evaluation in the emergency department: the PATCH-ED study. Emerg Med J. 2018;35(8):477-485. doi: 10.1136/emermed-2018-207570

15. Reynolds M, Passman R, Swindle J, et al. Comparative effectiveness of ambulatory monitors for arrhythmia diagnosis: a retrospective analysis of Medicare beneficiaries. Poster presented at: American College of Cardiology/World Congress of Cardiology (ACC/WCC) Annual Scientific Session; March 4-6, 2023; New Orleans, LA.

16. Rho R, Vossler M, Blancher S, Poole JE. Comparison of 2 ambulatory patch ECG monitors: The benefit of the P-wave and signal clarity. Am Heart J. 2018;203:109-117. doi: 10.1016/j.ahj.2018.03.022

17. Rooney MR, Soliman EZ, Lutsey PL, et al. Prevalence and Characteristics of Subclinical Atrial Fibrillation in a Community-Dwelling Elderly Population: The ARIC Study. Circ Arrhythm Electrophysiol. 2019;12(10):e007390. doi: 10.1161/CIRCEP.119.007390

18. Rosenberg MA, Samuel M, Thosani A, Zimetbaum PJ. Use of a noninvasive continuous monitoring device in the management of atrial fibrillation: a pilot study. Pacing Clin Electrophysiol. 2013;36(3):328-33. doi: 10.1111/pace.12053

19. Schreiber D, Sattar A, Drigalla D, Higgins S. Ambulatory cardiac monitoring for discharged emergency department patients with possible cardiac arrhythmias. West J Emerg Med. 2014;15(2):194-8. doi: 10.5811/westjem.2013.11.18973

20. Schultz KE, Lui GK, McElhinney DB, et al. Extended cardiac ambulatory rhythm monitoring in adults with congenital heart disease: Arrhythmia detection and impact of extended monitoring. Congenit Heart Dis. 2019;14(3):410-418. doi: 10.1111/chd.12736

21. Solomon MD, Yang J, Sung SH, et al. Incidence and timing of potentially high-risk arrhythmias detected through long term continuous ambulatory electrocardiographic monitoring. BMC Cardiovasc Disord. 2016;16:35. doi: 10.1186/s12872-016-0210-x

22. Steinhubl SR, Waalen J, Edwards AM, et al. Effect of a Home-Based Wearable Continuous ECG Monitoring Patch on Detection of Undiagnosed Atrial Fibrillation: The mSToPS Randomized Clinical Trial. JAMA. 2018;320(2):146-155. doi: 10.1001/jama.2018.8102

23. Steinhubl SR, Waalen J, Sanyal A, et al. Three year clinical outcomes in a nationwide, observational, siteless clinical trial of atrial fibrillation screening-mHealth Screening to Prevent Strokes (mSToPS). PLoS One. 2021;16(10):e0258276. doi: 10.1371/journal.pone.0258276

24. Tsang JP, Mohan S. Benefits of monitoring patients with mobile cardiac telemetry (MCT) compared with the Event or Holter monitors. Med Devices (Auckl). 2013;7:1-5. doi: 10.2147/MDER.S54038

25. Tung CE, Su D, Turakhia MP, Lansberg MG. Diagnostic Yield of Extended Cardiac Patch Monitoring in Patients with Stroke or TIA. Front Neurol. 2015;5:266. doi: 10.3389/fneur.2014.00266

26. Turakhia MP, Hoang DD, Zimetbaum P, et al. Diagnostic utility of a novel leadless arrhythmia monitoring device. Am J Cardiol. 2013;112(4):520-4. doi: 10.1016/j.amjcard.2013.04.017

27. Turakhia MP, Ullal AJ, Hoang DD, et al. Feasibility of extended ambulatory electrocardiogram monitoring to identify silent atrial fibrillation in high-risk patients: the Screening Study for Undiagnosed Atrial Fibrillation (STUDY-AF). Clin Cardiol. 2015;38(5):285-92. doi: 10.1002/clc.22387

28. Waalen J, Edwards AM, Sanyal A, et al. Healthcare resource utilization following ECG sensor patch screening for atrial fibrillation. Heart Rhythm O2. 2020;1(5):351-358. doi: 10.1016/j.hroo.2020.09.005

29. Wineinger NE, Barrett PM, Zhang Y, et al. Identification of paroxysmal atrial fibrillation subtypes in over 13,000 individuals. Heart Rhythm. 2019;16(1):26-30. doi: 10.1016/j.hrthm.2018.08.012