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Long-Term Ambulatory Cardiac Monitoring (Outpatient Cardiac Telemetry, Implantable Cardiac Rhythm Event Monitors, and Intracardiac Ischemia Detection Systems)

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Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

NOTE 1: This medical policy **DOES NOT FOCUS** on the following cardiac monitoring systems:

- Patient-activated or auto-activated external ambulatory event monitors,
- Holter monitors, or
- Zio® Patch/Zio XT.

Outpatient Cardiac Telemetry

Outpatient cardiac telemetry/mobile cardiac telemetry (OCT/MCT; e.g., Mobile Cardiac Outpatient Telemetry™ [MCOT™] system by CardioNet®, HEARTLink II™, Zio AT ECG Monitoring System, etc.) for up to 30 days **may be considered medically necessary** in the following situations:

- Monitoring of a suspected atrial fibrillation (AF) arrhythmia and following a noninvasive ambulatory cardiac monitoring of no less than 14 continuous days that is inconclusive or non-diagnostic (e.g., patch monitors, external event monitors); ***OR***

- Monitoring for a cryptogenic stroke with suspected occult AF as the cause of the stroke; ***OR***
- Monitoring the AF arrhythmia status following an ablation procedure.

Other uses of OCT, including any form of cardiac telemetry, (e.g., Mobile Cardiac Outpatient Telemetry™ [MCOT™] system by CardioNet®, HEARTLink II™, Zio AT ECG Monitoring System, etc.), including a smartwatch system, **are considered experimental, investigational and/or unproven**.

Implantable Cardiac Rhythm Event Monitors

The use of **implantable** cardiac rhythm/implantable loop recorders (ILRs) event monitors, either patient-activated or auto-activated **may be considered medically necessary *ONLY*** in the following situations:

- In the small subset of individuals who experience recurrent symptoms so infrequently that a prior trial of a noninvasive ambulatory cardiac monitoring of not less than 14 continuous days without a symptom is inconclusive or non-diagnostic (e.g., patch monitors, external event monitors); ***OR***
- In individuals who require long-term monitoring for AF or possible AF; ***OR***
- In individuals who are ≥ 40 years of age **and** require long-term monitoring for cryptogenic stroke when **ALL** the following tests, evaluated by a neurologist, have established the diagnosis of a prior cryptogenic ischemic stroke:
  - Brain magnetic resonance imaging or computed tomography (CT), **and**
  - 12-lead electrocardiogram (ECG) for AF detection, **and**
  - 24-hour ECG monitoring for AF detection (e.g., Holter monitor), **and**
  - Transesophageal echocardiography or transthoracic echocardiography, **and**
  - CT angiography (head and neck) or magnetic resonance angiography (head and neck) to rule out other causes of stroke.

Other uses of ILR event monitors **are considered experimental, investigational and/or unproven**, including but not limited to:

- Monitoring asymptomatic patients with risk factors for arrhythmias;
- Monitoring effectiveness of antiarrhythmic medications;
- Detection of myocardial ischemia by detecting ST segment changes.

Permanent Implantable Continuous Intracardiac Ischemia Detection System

The use of permanent **implantable** continuous intracardiac ischemia detection or monitoring system (e.g., AngelMed® Guardian™ System) **is considered experimental, investigational and/or unproven**.

Policy Guidelines

None.

Description

Various devices are available for outpatient cardiac rhythm monitoring. These devices differ in the types of monitoring leads used, the duration and continuity of monitoring, the ability to detect arrhythmias without patient intervention, and the mechanism of delivering the information from patient to clinician. These devices may be used to evaluate symptoms suggestive of arrhythmias (e.g., syncope, palpitations), and may be used to detect atrial fibrillation (AF) in patients who have undergone cardiac ablation of AF or who have a history of cryptogenic stroke.

Cardiac Arrhythmias

Cardiac monitoring is routinely used in the inpatient setting to detect acute changes in heart rate or rhythm that may need urgent response. For some conditions, a more prolonged period of monitoring in the ambulatory setting is needed to detect heart rate or rhythm abnormalities that may occur infrequently. These cases may include the diagnosis of arrhythmias in patients with signs and symptoms suggestive of arrhythmias as well as the evaluation of paroxysmal AF.

Cardiac arrhythmias may be suspected because of symptoms suggestive of arrhythmias, including palpitations, dizziness, or syncope or presyncope, or because of abnormal heart rate or rhythm noted on exam. A full discussion of the differential diagnosis and evaluation of each of these symptoms is beyond the scope of this policy, but some general principles on the use of ambulatory monitoring are discussed.

Arrhythmias are an important potential cause of syncope or near syncope, which in some cases may be described as dizziness. An electrocardiogram (ECG) is generally indicated whenever there is suspicion of a cardiac cause of syncope. Some arrhythmic causes will be apparent on ECG. However, for patients in whom an ECG is not diagnostic, longer monitoring may be indicated. The 2009 joint guidelines from the European Society of Cardiology and 3 other medical specialty societies suggested that, in individuals with clinical or ECG features suggesting an arrhythmic syncope, ECG monitoring is indicated; the guidelines also stated that the "duration (and technology) of monitoring should be selected according to the risk and the predicted recurrence rate of syncope." (1) Similarly, guidelines from the National Institute for Health and Care Excellence (2023) on the evaluation of transient loss of consciousness, have recommended the use of an ambulatory ECG in individuals with a suspected arrhythmic cause of syncope. The type and duration of monitoring recommended is based on the individual's history, particularly the frequency of transient loss of consciousness. (2) The Holter monitor (HM) is recommended if transient loss of consciousness occurs several times a week. If the frequency of transient loss of consciousness is every 1 to 2 weeks, an external event recorder is recommended; and if the frequency is less than once every 2 weeks, an implantable event recorder is recommended.

Similar to syncope, the evaluation and management of palpitations is patient-specific. In cases where the initial history, examination, and ECG findings are suggestive of an arrhythmia, some form of ambulatory ECG monitoring is indicated. A position paper from the European Heart Rhythm Association (2011) indicated that, for individuals with palpitations of unknown origin

who have clinical features suggestive of arrhythmia, referral for specialized evaluation with consideration for ambulatory ECG monitoring is indicated. (3)

Atrial Fibrillation Detection

AF is the most common arrhythmia in adults. It may be asymptomatic or be associated with a broad range of symptoms, including lightheadedness, palpitations, dyspnea, and a variety of more nonspecific symptoms (e.g., fatigue, malaise). It is classified as paroxysmal, persistent, or permanent based on symptom duration. Diagnosed AF may be treated with antiarrhythmic medications with the goal of rate or rhythm control. Other treatments include direct cardioversion, catheter-based radiofrequency- or cryo-energy-based ablation, or 1 of several surgical techniques, depending on the patient's comorbidities and associated symptoms.

Stroke in AF occurs primarily as a result of thromboembolism from the left atrium. The lack of atrial contractions in AF leads to blood stasis in the left atrium, and this low flow state increases the risk of thrombosis. The area of the left atrium with the lowest blood flow in AF, and therefore the highest risk of thrombosis, is the left atrial appendage. Multiple clinical trials have demonstrated that anticoagulation reduces the ischemic stroke risk in patients at moderate- or high-risk of thromboembolic events. Oral anticoagulation in patients with AF reduces the risk of subsequent stroke and is recommended by American Heart Association (AHA), American College of Cardiology (ACC), and Heart Rhythm Society (HRS) (2014) joint guidelines on patients with a history of stroke or transient ischemic attack. (4)

Ambulatory ECG monitoring may play a role in several situations in the detection of AF. In patients who have undergone ablative treatment for AF, if ongoing AF can be excluded with reasonable certainty, including paroxysmal AF which may not be apparent on ECG during an office visit, anticoagulation therapy could potentially be stopped. In some cases where identifying paroxysmal AF is associated with potential changes in management, longer term monitoring may be considered. There are well-defined management changes that occur in patients with AF. However, until relatively recently the specific role of long-term (i.e., >48 hours) monitoring in AF was not well-described.

Patients with cryptogenic stroke are often monitored for the presence of AF because AF is estimated to be the cause of cryptogenic stroke in more than 10% of patients, and AF increases the risk of stroke. (5, 6) Paroxysmal AF confers an elevated risk of stroke, just as persistent and permanent AF does. In individuals with a high-risk of stroke, particularly those with a history of ischemic stroke that is unexplained by other causes, prolonged monitoring to identify paroxysmal AF has been investigated.

Cardiac Rhythm Ambulatory Monitoring Devices

Ambulatory cardiac monitoring with a variety of devices permits the evaluation of cardiac electrical activity over time, in contrast to a static ECG, which only permits the detection of abnormalities in cardiac electrical activity at a single point in time.

A HM is worn continuously and records cardiac electrical output continuously throughout the recording period. HMs are capable of recording activity for 24 to 72 hours. Traditionally, most HMs have 3 channels based on 3 ECG leads. However, some currently available HMs have up to 12 channels. HMs are an accepted intervention in a variety of settings where a short period (24 to 48 hours) of comprehensive cardiac rhythm assessment is needed (e.g., suspected arrhythmias when symptoms [syncope, palpitations] are occurring daily).

Various classes of devices are available for situations where longer monitoring than can be obtained with a traditional HM is needed. Because there may be many devices within each category, a comprehensive description of each is beyond our scope. Devices vary in how data are transmitted to the location where the ECG output is interpreted. Data may be transmitted via cellular phone or landline, or by direct download from the device after its return to the monitoring center. The device classes are described in Table 1.

Table 1. Ambulatory Cardiac Rhythm Monitoring Devices – Telemetry or Implantable ONLY

Device Class	Purpose and Description	Example Devices
Outpatient Cardiac Telemetry (OCT) or Mobile Cardiac Telemetry (MCT)	The purpose of mobile OCT monitoring is to immediately capture a cardiac anomaly and provide more information on AF burden. Continuously recording or auto-triggered memory loop devices that transmit data to a central recording station with real-time monitoring and analysis.	• CardioNet MCOT (BioTelemetry) • LifeStar Mobile Cardiac Telemetry (LifeWatch Services) • Zio AT (iRhythm) • SmartCardia 7L (SmartCardia)
Implantable Cardiac Rhythm Event Monitors or Memory Loop Recording Devices (ILR; patient- or auto-triggered).	The purpose of ILRs in patients with signs or symptoms suggestive of arrhythmia with infrequent symptoms is to provide an alternative method of arrhythmia detection. Devices similar in design to external memory loop devices but implanted under the skin in the precordial region.	• Auto-triggered or patient-triggered: Reveal® XT ICM (Medtronic) and Confirm Rx Insertable Cardiac Monitor (Abbott) • Auto-triggered: BioMonitor, Biotronik

There are also devices that combine features of multiple classes. For example, the LifeStar ACT Ex Holter (LifeWatch Services) is a 3-channel HM but is converted to a mobile cardiac telemetry system if a diagnosis is inconclusive after 24 to 48 hours of monitoring. The BodyGuardian® Heart Remote Monitoring System (Preventice Services) is an external auto-triggered memory loop device that can be converted to a real-time monitoring system. The eCardio Verite™

system (eCardio) can switch between a patient-activated event monitor and a continuous telemetry monitor. The Spiderflash-T (LivaNova) is an example of an external auto-triggered or patient-triggered loop recorder, but like the Zio Patch, can record 2 channels for 14 to 40 days.

Implantable Continuous Intracardiac Ischemia Monitoring
The real-time permanent implantable ischemia detection system (IIDS) device is designed to detect rapid ST segment changes (ST-shifts) in the heart rhythm that may signify major cardiac events, such as acute coronary syndrome (ACS) that may create cardiac artery occlusions caused by life-threatening vulnerable plaque ruptures. ACS is a set of signs and symptoms that may result in decreased blood flow to coronary arteries. (7, 64) ACS is commonly associated with 3 clinical manifestations, named according to the appearance of the ECG: ST elevation myocardial infarction (STEMI, 30%), non-ST elevation myocardial infarction (NSTEMI, 25%), or unstable angina (38%) There can be some variations as to which forms of myocardial infarction (MI) are classified under acute coronary syndrome. The use of this device is proposed to reduce the time from onset of an ischemic event to presentation in an emergency room, with potential clinical benefits of more efficient emergent care.

There are 3 components of the IIDS monitor system, the first is the implantable medical device (IMD) which monitors the electrical activity (electrogram) of the heart and provides vibrations if changes are detected which sends an alert to the second component. The second component is the external device (EXD) which sets off lights and alarms when the alerts from the IMD are received, indicating the patient may need to seek medical attention. The third component is the programmer which collects and stores the data from the IMD. (7, 64) Therefore, once a ST-shift is detected, the IIDS will alert the patient to seek medical care by delivering a series of vibratory, auditory, and visual warnings, using Bluetooth technology with a pager-like device continuously worn by the patient. This IMD uses a standard pacemaker intracardiac lead positioned in the right ventricular apex. In addition to detecting acute ST changes and alerting the patient to seek medical attention, the device stores ECG traces for later analysis by the physician.

Regulatory Status
Regarding devices used to monitor specific arrhythmia conditions, such as telemetry or implantable, several are defined within the Description section above for informational purposes. As there are many devices within each category, a comprehensive description of individual devices is beyond the scope of this medical policy. The U.S. Food and Drug Administration (FDA) product codes include: DSH, DXH, DQK, DSI, MXD, MHX.

The FDA approved the AngelMed® Guardian™ System, from Angel Medical Systems, Tinton Falls, N.J., under the premarket approval (PMA) process on April 9, 2018. The device is indicated for use in patients who have had prior ACS events and who remain at high risk for recurrent ACS events, as an implantable cardiac monitor with patient alerting. (7) FDA Product Code: QBI.

Rationale

Medical policies assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

This medical policy is structured around 3 circumstances:

1. How is real-time outpatient cardiac telemetry (OCT) monitoring associated with improved outcomes?
2. How are implantable cardiac rhythm event monitors associated with improved outcomes?
3. How are implantable intracardiac ischemia detection systems (IIDS) associated with improved outcomes?

MONITORING OF ATRIAL FIBRILLATION (AF) ARRHYTHMIAS

Long-Term Cardiac Rhythm Event Monitors or OCT in the Detection of AF Arrhythmias

AF can be diagnosed on an electrocardiogram (ECG/EKG) or on Holter monitoring in individuals with suspected AF; however, a single ECG or short-term Holter monitor (HM) may not reliably exclude paroxysmal AF. In some cases, where identifying paroxysmal AF is associated with potential changes in management, longer term monitoring may be considered. There are well-defined management changes that occur in patients with AF. However, until relatively recently the specific role of long-term (i.e., >48 hours) monitoring in AF was not well-described.

For some of the ambulatory event monitors (AEMs) monitors discussed herein, including those that include real-time monitoring and analysis, the technologies represent an enhancement to existing technology and are intended to improve outcomes compared with event monitors. As such, to demonstrate an improvement in health outcomes, there must be a clinically significant incremental benefit when the additional technology, such as real-time monitoring, is added.

The rationale section will focus on clinical situations for which the use of long-term AEMs may

be associated with improved health outcomes in the detection of AF:

- The use of long-term AEMs for the detection of AF in patients following catheter ablation, for which management (use of anticoagulation therapy) may be changed based on AF detection.
- The use of long-term AEMs for the detection of AF in patients following cryptogenic stroke, for which management (use of anticoagulation therapy) may be changed based on AF detection.
- The use of long-term AEMs for the detection of AF in asymptomatic patients.

Clinical Context and Test Purpose

To address whether long-term outpatient cardiac telemetry (OCT) or implantable AEMs will be effective to detect AF following non-diagnostic AEM, monitoring for a cryptogenic stroke or following an ablation procedure.

The purpose of long-term AEM/OCT in patients who have possible signs and/or symptoms of AF arrhythmia is to provide an alternative detection method for AF.

The following PICO was used to select literature to inform this policy (see Table 2).

Table 2. PICO to Assess AF Arrhythmia Using Long-Term AEMs

PICO	Review Assessment
Populations	The relevant population of interest is those who have signs and/or symptoms of AF arrhythmia.
Interventions	The therapy being considered is long-term AEMs/outpatient cardiac telemetry worn continuously, automatically sending data to a monitoring center for analysis and response, which is longer than the Holter monitor.
Comparators	Alternative AF detection methods that are used include an ECG or 24- to 48-hour Holter monitoring. An ECG provides information on cardiac electrical activity at 1 point in time. A Holter monitor is worn continuously and records cardiac electrical output continuously throughout the recording period. Holter monitors are capable of recording activity for 24 to 72 hours.
Outcomes	The general outcome of interest is diagnostic yield of the monitors in detecting AF arrhythmias. To measure incremental benefits of the long-term ambulatory event monitors/outpatient cardiac telemetry worn continuously by the patient.

PICO: populations, interventions, comparators, outcomes; AF: atrial fibrillation; AEMs: ambulatory event monitors; electrocardiogram: ECG.

Study Selection Criteria

For the evaluation of clinical validity of long-term AEMs/OCT for patients with possible AF arrhythmia symptoms, studies that met the following criteria were considered:

- To assess the clinical validity, studies should report sensitivity, specificity, positive and negative predictive values. Alternatively, studies reporting on diagnostic yield are informative.

- To assess the clinical utility, studies should demonstrate how results of the tests impacted treatment decisions and overall management of the patient.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse). Below are studies providing evidence on the diagnostic yield of long-term AEMs/OCT when monitoring to detect AF following non-diagnostic AEM, monitoring for a cryptogenic stroke or following an ablation procedure.

OCT Monitoring of a Suspected AF Arrhythmia and Following a Non-Diagnostic AEM

Newer devices are available that record cardiac rhythms continuously for longer periods of time than traditional HMs. Several studies have evaluated the diagnostic yield of continuous monitoring for more than 48 hours, either directly through comparison with Holter monitoring or indirectly by calculating the proportion of arrhythmias detected in the first 48 hours of monitoring. The diagnostic yield of monitoring with external telemetry monitors depends on the underlying population, the inherent sensitivity of the device, and the duration of monitoring.

RCTs

An RCT by Rothman et al. (2007) compared Mobile Cardiac Outpatient Telemetry (MCOT) with standard event monitors (Table 3). (8) This trial involved 305 patients randomized to the LOOP recorder or to MCOT (CardioNet) and monitored for up to 30 days. Patients were recruited from 17 centers. Investigators and patients were not blinded to randomization assignment. Monitor strips and diagnoses were reviewed by an electrophysiologist blinded to the monitoring device assignment. Most patients in the LOOP recorder group had a patient-triggered event monitor. Only a subset of patients (n=50) had auto-trigger devices, thus precluding comparison between MCOT and auto-trigger devices. Analyses were conducted on patients completing at least 25 days of monitoring. The primary endpoint was either confirmation or exclusion of arrhythmic cause of the patient's symptoms. Arrhythmias were classified as either clinically significant or clinically insignificant. The diagnostic endpoint (confirmation or exclusion of arrhythmic cause of symptoms) was significantly different between the 2 groups (Table 4). The difference in rates was primarily due to detection of asymptomatic (not associated with simultaneous symptoms) arrhythmias in the MCOT group, symptoms consisting of rapid AF and/or flutter (15 patients versus 1 patient), and ventricular tachycardia (VT) defined as more than 3 beats and rate greater than 100 (14 patients versus 2 patients). These differences were thought to be clinically significant rhythm disturbances and the likely causes of the patients' symptoms. In this trial, median time to diagnosis in the total study population was 7 days in the MCOT group and 9 days in the LOOP group (Table 4). The trialists did not comment on the clinical impact (changes in management) of these findings in patients for whom the rhythm disturbance did not occur simultaneously with symptoms.

Table 3. Summary of RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions		Duration
					Active	Comparator	

Rothman et al. (2007) (8)	United States	17	NR	Patients with a high clinical suspicion of a malignant arrhythmia, with syncope, presyncope, or severe palpitations, and a non-diagnostic 24-hr Holter test	MCOT (Cardio-Net) n=134	Patient-activated external looping event monitor n=132	Confirmation of a diagnosis, up to 30 days

hr: hour; MCOT: mobile automated cardiac outpatient telemetry; NR: not reported; RCT: randomized controlled trial.

Table 4. Summary of RCT Results

Study	Confirmation or Exclusion of Arrhythmic Cause of Symptoms, n (%)	Confirmation or Exclusion of Arrhythmic Cause of Symptoms in Subgroup with Syncope, n (%)	Confirmation or Exclusion of Arrhythmic Cause of Symptoms in Subgroup Autotriggered Recorder, n (%)	Time to Diagnosis median (95% CI)
Rothman et al. (2007) (8)	263	113	50	263
MCOT	117 (88.0)	55 (88.7)	21 (87.5)	7 (4 to 11)
LOOP	98 (75.4)	35 (68.6)	12 (46.2)	9 (7 to 15)
p-value	.008	.008	.002	NR

CI: confidence interval; LOOP: looping event monitor; MCOT: mobile cardiac outpatient telemetry; NR: not reported; n: number; RCT: randomized controlled trial.

Observational Studies - Arrhythmia Detection

Derkac et al. (2017) retrospectively reviewed the BioTelemetry database of patients receiving ambulatory ECG monitoring, selecting patients prescribed OCT (n=69,977) and patients prescribed AT-LER, an auto-trigger looping event recorder (n=8513). (9) Patients were diagnosed with palpitations, syncope and collapse, AF, tachycardia, and/or transient ischemic attack (TIA). Patients given the OCT were monitored for an average of 20 days and patients given the AT-LER were monitored an average of 27 days. The diagnostic yield using OCT was significantly higher than that using AT-LER for several events: 128% higher for AF, 54% higher for bradycardia, 17% higher for ventricular pause, 80% higher for supraventricular tachycardia (SVT), and 222% higher for VT. Mean time to diagnosis for each asymptomatic arrhythmia was shorter for patients monitored by OCT than by AT-LER. There was no discussion of management changes or health outcomes based on monitoring results. Note, the authors were manufacturer

stakeholders.

Kadish et al. (2010) evaluated the frequency with which events transmitted by OCT represented emergent arrhythmias, thereby indirectly assessing the clinical utility of real-time outpatient monitoring. (10) Medical records from 26,438 patients who had undergone OCT during a 9-month period from a single service provider were retrospectively examined. During a mean monitoring period of 21 days, 21% (5459) had an arrhythmic event requiring physician notification. Of these, 1% (260) had an event that could be considered potentially emergent. These potentially emergent events included 120 patients with wide-complex tachycardia, 100 patients with sinus pauses of 6 seconds or longer, and 42 with sustained bradycardia at less than 30 beats per minute.

A number of uncontrolled case series have reported on arrhythmia detection rates of MOCT. (11-14) One study (Joshi et al. [2005]) described the outcomes of a consecutive case series of 100 patients. (11) Included patients had the following symptoms: palpitations (47%), dizziness (24%), or syncope (19%). Patients being evaluated for the efficacy of drug treatment (25%) were also included. Clinically significant arrhythmias were detected in 51% of patients, but half of these patients were asymptomatic. The authors commented that the automatic detection resulted in an increased diagnostic yield, but there was no discussion of its unique features (i.e., the real-time analysis, transmission, and notification of arrhythmia).

Observational Studies - AF Detection
In the largest study evaluating the diagnostic yield of OCT for AF, Favilla et al. (2015) evaluated a retrospective cohort of 227 patients with cryptogenic stroke or TIA who underwent 28 days of monitoring with OCT. (15) AF was detected in 14% (31/227) of patients, of whom 3 reported symptoms at the time of AF. Oral anticoagulation was initiated in 26 (84%) patients diagnosed with AF. Of the remaining 5 (16%) not on anticoagulation therapy, 1 had a prior history of gastrointestinal bleeding, 3 were unwilling to accept the risk of bleeding related to the use of anticoagulants, and 1 failed to follow-up.

Miller et al. (2013) retrospectively analyzed paroxysmal AF detection rates among 156 patients evaluated with OCT within 6 months of a cryptogenic stroke or TIA. (16) Over a median 21-day period of OCT monitoring (range, 1 to 30 days), AF was detected in 17.3% of patients. Mean time to first occurrence of AF was 9 days (range, 1 to 21 days).

Tayal et al. (2008) retrospectively analyzed patients with cryptogenic stroke who had not been diagnosed with AF by standard monitoring. (14) In this study, 13 (23%) of 56 patients with cryptogenic stroke had AF detected by OCT. Twenty-seven asymptomatic AF episodes were detected in the 13 patients; 23 of them were less than 30 seconds in duration. In contrast, Kalani et al. (2015) reported a diagnostic yield for AF of 4.7% (95% confidence interval [CI], 1.5% to 11.9%) in a series of 85 patients with cryptogenic stroke. (17) In this series, 82.4% of patients had completed transesophageal echocardiography, cardiac magnetic resonance imaging (MRI), or both, with negative results. Three devices were used and described as OCT devices: 34% received LifeStar ACT ambulatory cardiac telemetry, 41% received the LifeStar AF Express

autodetect looping monitor, and 25% received the Cardiomedix cardiac event monitor. While the authors reported that there was a system in place to transmit the data for review, it is unclear whether data were sent in "real-time."

Narasimha et al. (2018) published results of a study in which 33 patients wore both an external loop recorder (ELR) and a Kardia monitor to screen for AF during a period of 14 to 30 days. (18) Patients were 18 years or older, had palpitations less often than daily but more frequently than several times per month, and prior nondiagnostic ECGs. Exclusion criteria included myocardial infarction within the last 3 months, history of VT/fibrillation, unstable angina, and syncope. Study personnel viewed the Kardia monitor recordings once daily and a physician was contacted if a serious or sustained arrhythmia was detected. Patients were also monitored by the ELR company, which notified a physician on call when necessary. All 33 patients had a diagnosis using the Kardia monitor, and 24 patients received a diagnosis using the ELR (p=.001).

Dorr et al. (2019) compared the diagnostic accuracy of a smartwatch system with cardiologists' interpretation of an ECG in the diagnostic accuracy to detect AF. (19) The smartwatch system uses an algorithm to enable rhythm analysis of the photoplethysmographic (PPSG) signals. The population consisted of 508 hospitalized patients who had interpretable ECG and PPSG recordings. The PPSG algorithm compared with the cardiologists' diagnoses had a sensitivity of 94% and a specificity of 98%. A limitation of the study was that many of the recordings were excluded due to insufficient signal quality (148 of 672). The investigators concluded that detection of AF is feasible with a smartwatch, though signal quality issues need to be resolved and a broader population needs to be tested.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs. No RCTs were identified that evaluated the management of patients with and without mobile cardiac monitoring.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. Evidence for clinical validity consists of 1 RCT and several observational studies. The RCT reported a larger proportion of patients receiving a diagnosis in the OCT group compared with the LOOP group, though time to diagnosis was not significantly different. In addition, no studies demonstrated an incremental benefit of the real-time transmission and interpretation of data compared with the usual monitoring timeline.

Subsection Summary: OCT Monitoring of a Suspected AF Arrhythmia and Following a Non-

Diagnostic AEM

The available evidence has suggested that OCT is likely to be at least as good at detecting arrhythmias as AEM. Compared with AEM, OCT is associated with the theoretical advantage of real-time monitoring, permitting for emergent intervention for potentially life-threatening arrhythmias. One study reported that 1% of arrhythmic events detected on OCT during a mean monitoring period of 21 days per patient could be considered potentially emergent. However, no studies were identified that addressed whether the use of OCT is associated with differences in the management of or outcomes after these potentially emergent events. The addition of real-time monitoring to outpatient ambulatory monitoring is considered an enhancement to existing technology. Because OCT is as good as AEMs to detect AFs, the evidence does demonstrate a clinically significant incremental benefit for OCT. However, utilization of the smartwatch system has not shown any incremental benefit as a form of OCT, due to the lack of evidence and signal transmission quality.

Monitoring for a Cryptogenic Stroke with Suspected Occult AF as the Cause of the Stroke

Approximately 5% of individuals with cryptogenic stroke will have AF diagnosed on ECG and/or telemetry monitoring in the hospital. Individuals with a history of cryptogenic stroke who have had AF detected, are typically treated with anticoagulants. Studies comparing the use of continuous telemetry monitory at the bedside with Holter monitoring for individuals hospitalized for stroke or TIA have reported inconclusive results as to which is the preferred method for AF detection. (20, 21) Longer term ambulatory event monitoring has been shown to identify additional individuals with asymptomatic episodes, with rates of detection estimated at 6% to 26% of individuals. (5, 22, 16)

Systematic Reviews

Sposato et al. (2015) conducted a systematic review and meta-analysis of studies assessing rates of newly diagnosed AF after cryptogenic stroke or TIA based on cardiac monitoring, stratified into 4 sequential screening phases:

- Phase 1 (emergency department) consisted of admission ECG;
- Phase 2 (in-hospital) comprised serial ECG, continuous inpatient ECG monitoring, continuous inpatient cardiac telemetry, and in-hospital Holter monitoring;
- Phase 3 (first ambulatory period) consisted of ambulatory Holter monitoring; and
- Phase 4 (second ambulatory period) consisted of OCT, ELR, and ILR. (23)

In total, 50 studies with 11,658 patients met the inclusion criteria. Studies were mixed in their patient composition: 22 (28%) included only cryptogenic stroke cases, 4 (5%) stratified events into cryptogenic and non-cryptogenic, and 53 (67%) included unselected patient populations. The proportion of patients diagnosed with post-stroke AF during the ambulatory phases was 10.7% (95% CI, 5.6% to 17.2%) in phase 3, and 16.9% (95% CI, 13.0% to 21.2%) in phase 4. The overall AF detection yield after all phases of sequential cardiac monitoring was 23.7% (95% CI, 17.2% to 31.0%). In phase 4, there were no differences between the proportion of patients diagnosed with post stroke AF by OCT (15.3%; 95% CI, 5.3% to 29.3%), ELR (16.2%; 95% CI, 0.3% to 24.6%), or ILR (16.9%; 95% CI, 10.3% to 24.9%; p=.97).

Kishore et al. (2014) conducted a systematic review and meta-analysis of prospective observational studies and RCTs that have reported detection rates of newly diagnosed AF in patients with ischemic stroke or TIA who had had any cardiac monitoring for at least 12 hours. (24) Thirty-two studies were selected: 18 studies included patients with ischemic stroke only, 1 study included TIA only, and 13 studies included both ischemic stroke and TIA. Reviewers reported significant study heterogeneity. Among unselected patients (i.e., selected on the basis of stroke pathogenesis, age, or prescreening for AF), the detection rate of any new AF was 6.2% (95% CI, 4.4% to 8.3%); among selected patients, it was 13.4% (95% CI, 9.0% to 18.4%). In cryptogenic strokes, new AF was detected in 15.9% of patients (95% CI, 10.9% to 21.6%). Among selected patients, the AF detection rate during 24-hour Holter monitoring was 10.7% (95% CI, 3.4% to 21.5%), while the detection rate during monitoring beyond 24 hours (including more prolonged Holter monitoring, implantable and non-implantable loop recording, and OCT) was 14.7% (95% CI, 10.7% to 19.3%).

The Kishore et al. (2014) study and others suggest that longer periods of cardiac monitoring increase the likelihood of AF detection. However, many of these asymptomatic episodes of AF are brief and their relation to the preceding stroke uncertain. The ideal study to evaluate the role of cardiac monitoring in the management of patients with cryptogenic stroke would be trials that randomize patients to a strategy involving event monitoring or routine care with evaluation of rates of detection of AF and stroke-related outcomes.

RCTs

Five RCTs were identified that evaluated ambulatory monitoring in patients with cryptogenic stroke (Table 5). Two were small pilot trials. One small pilot RCT published by Kamel et al. (2013) randomized 40 patients with cryptogenic ischemic stroke or high-risk TIA to usual care or to 21 days of OCT. (25) There were no cases of AF detected in either group (Table 6).

A second small pilot trial published by Higgins et al. (2013) randomized 100 patients with ischemic stroke and no history of AF presenting within 7 days of a cryptogenic ischemic stroke to either standard care, which included 12-lead ECG, 24-hour Holter monitoring, and/or echocardiography, at the discretion of the treating practitioner, or to standard care plus cardiac event monitoring with Novacor R-test Evolution 3, an ELR device (Table 5). (26) Sustained AF (recorded for the complete 20-second rhythm strip after event triggering) was detected significantly more often with the ELR than with standard care at 14-day follow-up. The difference did not differ statistically at 90-day follow-up (Table 6).

Sanna et al. (2014) reported on results from the Cryptogenic Stroke and underlying times Fibrillation (CRYSTAL AF) trial, an RCT that evaluated whether long-term monitoring with implantable cardiac monitors (ICM[s]) in patients who had cryptogenic stroke would lead to changes in anticoagulant management and/or improved outcomes (Table 5). (27, 28) The trial randomized 441 patients to continuous monitoring with the Reveal XT ICM or routine care. Eligibility criteria included no known history of AF, cryptogenic stroke, or TIA with infarct, and no mechanism determined after a workup that included 12-lead ECG, 24-hour Holter monitoring, transesophageal echocardiography, computed tomography (CT) or magnetic

resonance angiography (MRA) of the head and neck, and hypercoagulability screening (for patients <55 years old). Analysis was intention-to-treat. Of the 441 patients randomized, 416 (94.3%) completed 6-month follow-up, 2 were lost to follow-up, 5 died, and 18 exited the trial before 6 months. Crossover occurred in 12 patients in the ICM group and 6 in the control group. AF was detected in 8.9% of the ICM group compared with 1.4% of the control group (hazard ratio [HR], 6.43; 95% CI, 1.90 to 21.74) (Table 6). Median time from randomization to detection of AF was 41 days (inter-quartile range, 14 to 84 days) in the ICM group and 32 days (inter-quartile range, 2 to 73 days) in the control group. Most AF episodes in the ICM group were asymptomatic (74%) compared with 33% in the control group. The rate of AF detection was similarly greater in the ICM group at the 12-month follow-up (Table 6). A majority of patients who had AF detected were prescribed anticoagulation therapy. Five (2.4%) of the 208 implantable cardiac monitors inserted were removed due to infection or erosion of the device pocket. Brachmann et al. (2016) reported 3-year follow-up results from the CRYSTAL AF trial. (29) At trial closure, 48 subjects had completed 3 years of follow-up (n=24 in each treatment group). By 3 years, the HR for detecting AF for ICM-monitored versus control patients was 8.8 (95% CI, 3.5 to 22.2; p<.001).

Gladstone et al. (2014) reported results from the Atrial Fibrillation in Patients with Cryptogenic Stroke study, an RCT that compared 30-day auto-triggered external loop cardiac event monitors with conventional 24-hour monitors for the detection of AF in patients with cryptogenic stroke (Table 5). (30) Patients were ages 55 years or older, with no known history of AF, and an ischemic stroke or TIA of undetermined cause within the prior 6 months. All patients underwent standard screening for AF with 1 or more ECGs and 1 or more 24-hour HMs. In total, 572 patients were randomized to an ELR (ER910AF Cardiac Event Monitor, Braemar) or to a 24-hour HM. Among intervention group subjects, 82% completed at least 3 weeks of monitoring. AF was detected in 45 (16.1%) of 280 patients in the intervention group compared with 9 (3.2%) of 277 patients in the control group (risk difference, 12.9 percentage points; 95% CI, 8.0 to 17.6; p<.001) (Table 6). At 90-day follow-up, patients in the intervention group (18.6%) were more likely to be treated with anticoagulants than those in the control group (11.1%; absolute treatment difference, 7.5 percentage points; 95% CI, 1.6 to 13.3; p=.01).

Kaura et al. (2018) compared monitoring with the Zio Patch to short-term Holter monitoring in 120 patients following TIA or ischemic stroke. (31) Patch-based monitoring was superior to standard monitoring for the detection of paroxysmal AF over the 90-day follow-up period (16.3% versus 2.1%; odds ratio, 8.0; 95% CI, 1.1 to 76.0; p=.026).

Table 5. Summary of RCT Characteristics for AEM for Cryptogenic Stroke

Study	Country	Sites	Dates	Participants	Interventions (n)	
					Active	Comparator
Kamel et al. (2013) (25)	U.S.	1	2009-2011	Cryptogenic ischemic stroke or high-risk TIA	OCT (20)	Standard (20)
Higgins et al. (2013) (26)	U.K.	2	2010-2011	Transient or persistent	ELR (50)	Standard (50)

				symptoms of acute TIA		
Sanna et al. (2014) (28) and Brachmann et al. (2016) (29)	Canada, Europe, U.S.	55	2009-2012	Cryptogenic ischemic stroke or TIA	ILR (221)	Standard (220)
Gladstone et al. (2014) (30)	Canada	16	NR	Cryptogenic ischemic stroke or TIA	ELR (280)	Standard (277)
Kaura et al. (2019) (31)	U.K.	2	NR	Cryptogenic ischemic stroke or TIA	Zio Patch (60)	Standard (60)

AEMs: ambulatory event monitors; ELR: external loop recorder; ILR: implantable loop recorder; NR: not reported; OCT: outpatient cardiac telemetry; RCT: randomized controlled trial; TIA: transient ischemic attack; U.S.: United States; U.K.: United Kingdom.

Table 6. Summary of RCT Results for AEMs for Cryptogenic Stroke

Study	FU	AF Detection			Additional Findings
		AEM, %	Standard, %	p-value	
Kamel et al. (2013) (25)	90 d	0	0	NS	• OCT identified AT in 2 patients (1 incorrectly labeled as AF by telemetry software) • OCT identified 2 non-sustained VT
Higgins et al. (2013) (26)	14 d 90 d	18 22	28	<0.05 0.09	• No difference between groups for recurrent stroke, TIA, or mortality
Sanna et al. (2014) (28); Brachmann et al. (2016) (29)	6 mo 12 mo 3 y	8.9 12.4 30	1.4 2.0 3.0	<.001 <.001 <.001	• Percent patients on oral anticoagulation therapy significantly higher in ILR group versus standard group • At 3-year follow-up, recurrent stroke or TIA occurred in 20 patients in ILR group and in 24 in standard group
Gladstone et al. (2014) (30)	90 d	16.1	3.2	<.001	• Atrial premature beats were identified in a

					regression model as a potential predictor of AF detection
Kaura et al. (2019) (31)	90 d	16.3	2.1	.026	• AF detection at 28 days was 14.0% (6 patients) in the Zio Patch group versus 2.1% (1 patient) in the standard group (p=.05)

AEM: ambulatory event monitor; AF: atrial fibrillation; AT: atrial tachycardia; d: day(s); FU: follow-up; ILR: implantable loop recorder; mo: month(s); NS: not specified; OCT: outpatient cardiac telemetry; RCT: randomized controlled trial; TIA: transient ischemic attack; VT: ventricular tachycardia; y: year(s).

Non-randomized Studies

Non-randomized and non-comparative studies published before the RCTs described above have reported on AF detection rates after cryptogenic stroke and long-term monitoring with various devices, including ILRs, (6, 32, 33) and continuous monitors with longer recording periods, (34) along with a pilot study evaluating the Zio Patch for AF detection poststroke. (35)

Subsection Summary: Monitoring for a Cryptogenic Stroke with Suspected Occult AF as the Cause of the Stroke

Randomized studies, including 2 large RCTs, have demonstrated that long-term monitoring is associated with higher rates of AF detection compared with HMs among patients with cryptogenic stroke. Because most patients with a history of stroke who have AF detected will be treated with anticoagulation, and because anticoagulation is an effective treatment for stroke prevention, it can be concluded that longer term monitoring of patients with cryptogenic stroke will improve outcomes. Because different long-term monitoring devices were used across the studies, the specific type of monitoring associated with the best outcomes is not established.

Long-Term Ambulatory Cardiac Monitoring for Patients with AF Following Ablation

All individuals treated with ablation are given anticoagulation for up to 3 months post-procedure, with many individuals remaining on long-term anticoagulation. In individuals with an apparently successful ablation who do not show signs or symptoms of recurrent AF at time periods longer than 3 months postablation, a decision whether to continue treatment with anticoagulants needs to be made. Studies have demonstrated that late recurrences are not uncommon after ablation and that these recurrent episodes are often asymptomatic. (36, 37) However, the presence of recurrent episodes of AF is a predictor of future thromboembolic events. In a large observational study of 565 individuals postablation, Chao et al. (2011) found the 2 major predictors of thromboembolism were the $CHADS_2$ (Congestive Heart Failure, Hypertension, Age, Diabetes Mellitus, and Stroke History) score and the presence of recurrent episodes of AF. (38)

RCTs

In a prospective, randomized study, Kapa et al. (2013) compared ILR with conventional

transtelephonic recorders in the assessment of arrhythmia burden after catheter ablation. (39) Forty-four patients were enrolled and randomized; all patients received the ILR postablation. Six patients were excluded due to requests for device removal or loss to follow-up. During the first 6 months after ablation, all subjects underwent conventional monitoring that consisted of twice daily 1-minute pulse rate assessments by the patient and three 30-day transtelephonic monitoring periods. At 6 months postablation, patients were allocated to the randomization arm (on a 1:1 basis at initial enrollment) of either the ILR (transmission of data every 31 days) or conventional monitoring (twice daily 1-minute pulse-rate assessment, 1 transtelephonic recording for 30 days at month 11). At 6 months postablation, conventional monitoring detected AF in 7 (18%) of 38 patients and the ILR confirmed AF in all these patients. ILR monitoring also detected AF in an additional 11 (29%) patients. During the subsequent 6-month period, 5 of 18 patients in the conventional monitoring arm refused ongoing monitoring due to discomfort and lifestyle restrictions; of the remaining 13, 5 (38%) had a recurrence of AF. In the ILR group, 5 (25%) of 20 patients had recurrence of AF. During the randomization period, 71% of patients in the ILR group discontinued their antiarrhythmic drugs compared with 44% in the conventional monitoring group over the randomization period (p=.04).

Observational Studies

Reporting on the prospective DISCERNAF (Discerning Symptomatic and Asymptomatic Episodes Pre-and Post-Radiofrequency Ablation of AF) study, Verma et al. (2013) evaluated the incidence of asymptomatic AF episodes for 3 months before and 18 months after ablation in 50 patients implanted with a cardiac monitor. (40) Patients were instructed to keep a standardized diary record of arrhythmia symptoms. Asymptomatic AF recurrences were defined as ICM events lasting 2 minutes or longer, without a corresponding diary entry. Based on diary reporting of symptoms, 29 (58%) of 50 patients were arrhythmia-free after ablation; based on monitor recordings from intermittent (every 3 month) ECG or HM, 28 (56%) patients were arrhythmia-free postablation. Patient detection of symptoms underestimates the AF occurrence rate following ablation, with 12% of patients having arrhythmias that were only detected through monitoring.

Several observational studies have followed patients who stopped anticoagulation after a comprehensive evaluation, which included ambulatory monitoring that indicated the patient had a low-risk for recurrent episodes. These patients experienced a low subsequent rate of thromboembolic events. In 1 study, Themistoclakis et al. (2010) evaluated 3355 patients from 5 clinical centers, of whom 2692 discontinued anticoagulation at 3 to 6 months postablation and 663 continued anticoagulation medications. (41) During a mean follow-up of 28 months, 2 (0.07%) patients who discontinued anticoagulation experienced an ischemic stroke. This rate did not differ significantly from the stroke rate in patients who continued anticoagulation (0.45%). In addition, the adverse event rate of major hemorrhage was lower for patients who discontinued anticoagulation (0.04%) compared with those who continued (2%; p<.001).

Subsection Summary: Long-Term Ambulatory Cardiac Monitoring for Patients with AF Following Ablation

Evidence includes an RCT and several observational studies that make a strong indirect

argument that long-term monitoring for asymptomatic episodes of AF with AEMs will lead to changes in management with long-term anticoagulation. One study reported that patients, who discontinued anticoagulation therapy after ambulatory monitoring was negative for recurrent episodes, experienced a low rate of stroke similar to patients who remained on anticoagulation therapy. In addition, patients discontinuing anticoagulants experienced fewer major hemorrhages. These changes in management based on ambulatory monitoring are likely to improve outcomes.

IMPLANTABLE LOOP RECORDERS (ILRS)

This section discusses the use of ILRs, with a focus on clinical situations when use of an ILR at the beginning of a diagnostic pathway is indicated. It is expected that a longer period of monitoring with any device category is associated with a higher diagnostic yield. A progression in diagnostics, from an external event monitor to ILR, in cases where longer monitoring is needed is considered appropriate. However, there may be situations where it is sufficiently likely that long-term monitoring will be needed and that an ILR as an initial strategy may be reasonable.

Systematic Reviews

Solbiati et al. (2017) conducted a systematic review and meta-analysis on the diagnostic yield of ILRs in patients with unexplained syncope. (42) The literature search, conducted through November 2015, identified 49 studies, published between 1998 and 2015, enrolling a total of 4381 patients. The methodologic quality of the studies was assessed using QUADAS (QUality Assessment of Diagnostic Accuracy Studies) and QUADAS-2. The diagnostic yield of ILR, defined as the proportion of patients in which ILR was useful in determining a syncope diagnosis was 44% (95% CI, 40% to 48%; I^2=80%). Diagnoses included arrhythmic syncope, ventricular arrhythmia, supraventricular arrhythmia, and bradyarrhythmia. Reviewers noted that an important analytic limitation was the considerable heterogeneity among studies, partly because definitions of syncope and methods to assess unexplained syncope were inconsistent.

Burkowitz et al. (2016) conducted a systematic review and meta-analysis of ILRs in the diagnosis of syncope and the detection of AF. (43) For syncope diagnosis, the review identified 3 RCTs comparing ILRs with a conventional diagnosis strategy (Holter monitoring). In pooled analysis, an ILR diagnosis strategy was associated with a higher likelihood of the end point of diagnostic yield (relative risk [RR], 4.17; 95% CI, 2.57 to 6.77; I^2=14%). The RCTs (Da Costa et al. [2013], [44] Farwell et al. [2004], [45] and Krahn et al. [2001] [46]) are described below.

Afzal et al. (2015) reported on a systematic review and meta-analysis of studies comparing ILRs with wearable AEMs for prolonged outpatient rhythm monitoring after cryptogenic stroke. (47) Reviewers included 16 studies (total n=1770 patients): 3 RCTs and 13 observational studies. For ILR-monitored patients, the median monitoring duration was 365 days (range, 50 to 569 days), while for wearable device-monitored patients, the median monitoring duration was 14 days (range, 4 to 30 days). Compared with wearable AEMs, ILRs were associated with significantly higher rates of AF detection (23.3% versus 13.6%; odds ratio, 4.54; 95% CI, 2.92 to 7.06; p<.05).

RCTs

Podoleanu et al. (2014) reported on results of an open-label RCT comparing 2 strategies for evaluating syncope: an experimental strategy involving the early use of an ILR and a conventional evaluation strategy excluding an ILR (Table 7). (48) The trial included patients who had a single syncope (if severe and recent) or at least 2 syncope episodes in the past 12 months. The syncope had to be unexplained at the end of clinical examination and who had a workup with 12-lead ECG, echocardiography, and head-up tilt-test. Patients randomized to ILR received the Reveal® or Reveal® Plus device. After 14 months of follow-up, a definitive cause of syncope was established more frequently in the ILR group than in the standard care group (Table 8). Arrhythmic causes of syncope in the ILR group included 2 (5%) cases of atrioventricular (AV) block, 4 (10%) cases of sinus node disease, 1 (2.5%) case of AF, 1 (2.5%) case of ventricular fibrillation, and 3 (8%) other tachycardias. In the conventionally managed group, 8 patients had a diagnosis of presumed reflex syncope.

Da Costa et al. (2013) compared use of an ILR with a conventional follow-up strategy in 78 patients with a first episode of syncope (Table 7). (44) A significant number of patients had cardiomyopathy (23%), AF (15.4%), and/or bundle branch block (58%) on ECG. Twenty-one (27%) patients had at least 1 arrhythmia detected, with a significant difference in the detection rate for the ILR group compared with the conventional follow-up group (Table 8).

Giada et al. (2007) conducted an RCT assessing 2 diagnostic strategies in 50 patients with infrequent (≤1 episode per month) unexplained palpitations: an ILR strategy (n=26) and a conventional strategy (n=24) including 24-hour HM, 4 weeks of ambulatory ECG monitoring with an external recorder, and an electrophysiologic study if the 2 prior evaluations were negative (Table 7). (49) Prior cardiac evaluation in eligible patients included standard ECG and echocardiography. Rhythm monitoring was considered diagnostic when a symptom-rhythm correlation was demonstrated during spontaneous palpitations that resembled pre-enrollment symptoms. In the conventional strategy group, a diagnosis was made in 5 (21%) subjects, after a mean time to diagnosis of 36 days, based on external ECG monitoring in 2 subjects and electrophysiologic studies in 3 subjects. In the ILR group, a diagnosis was made in 19 subjects after a mean time to diagnosis of 279 days (Table 8).

Farwell et al. (2004) reported on an RCT comparing the diagnostic yield of an ILR (Reveal® Plus) with a conventional diagnostic strategy in 201 patients with unexplained syncope (Table 7). (45) Eligible patients were evaluated at a single institution for recurrent syncope and had no definitive diagnosis after a basic initial workup (including 12-lead ECG, Holter monitoring in patients with suspected cardiac syncope, upright cardiac sinus massage, and tilt-table testing). At last follow-up, more loop recorder patients had an ECG diagnosis than control patients (HR for ECG diagnosis, 8.93; 95% CI, 3.17 to 25.19; p<.001) (Table 8). Seven of the loop recorder patients were diagnosed with the device's auto-trigger feature. In the loop recorder group, 34 patients had an ECG-directed therapy initiated (versus 4 in the control group; HR=7.9; 95% CI, 2.8 to 22.3). No device-related adverse events were reported.

An earlier RCT by Krahn et al. (2001) compared a conventional monitoring strategy (ELR

monitoring for 2 to 4 weeks, followed by tilt-table and electrophysiologic testing) with at least 1 year of monitoring using an ILR in 60 subjects with unexplained syncope (n=30 per group) (Table 7). (46) Eligible patients had a previous clinical assessment, at least 24 hours of continuous ambulatory monitoring or inpatient telemetry, and a transthoracic echocardiogram. A diagnosis was made in 20% of those in the conventional monitoring arm and in 52% of those in the ILR arm (Table 8).

Table 7. Summary of RCT Characteristics for ILRs for Arrhythmia

Study	Country	Sites	Dates	Participants	Interventions (n)	
					Active	Comparator
Podoleanu et al. (2014) (48)	France	13	2004-2008	Single recent syncope or 2 in past 12 mo	ILR (39)	Standard (39)
Da Costa et al. (2013) (44)	France	Multiple, NS	2005-2010	Single syncope	ILR (41)	Standard (37)
Giada et al. (2007) (49)	Italy	Multiple, NS	NR	Unexplained palpitations	ILR (26)	Standard (24)
Farwell et al. (2004) (45)	England	1	2000-2001	≥2 unexplained syncope in past 12 mo	ILR (103)	Standard (98)
Krahn et al. (2001) (46)	England	1	NR	Single or recurrent unexplained syncope	ILR (27)	ELR (30)

ELR: external loop recorder; ILR: implantable loop recorder; mo: month(s); NR: not reported; NS: not specified; RCT: randomized controlled trial.

Table 8. Summary of RCT Results for ILRs for Arrhythmia

Study	FU	Diagnosis Made, n			Additional Findings
		ILR	Standard	p-value	
Podoleanu et al. (2014) (48)	14 mo	18 (46)	2 (5)	<.001	• Advanced cardiology tests performed less frequently in ILR group versus standard (p=.05) • No difference in QOL
Da Costa et al. (2013) (44)	27 mo[a]	15 (37)	4 (11)	.02	• Earlier diagnosis in ILR group permitted earlier pacemaker implantation. However, earlier implantation did not improve survival

					(potentially due to small sample)
Giada et al. (2007) (49)	≥12 mo	19 (73)	5 (21)	<.001	• 9 of 19 patients with negative results with standard care crossed over to ILR and 6 of them received a diagnosis
Farwell et al. (2004) (45)	≥6 mo	34 (33)	4 (4)	<.001	• ECG-directed therapy was initiated quicker in the ILR group • No difference in syncopal episodes, mortality, or QOL
Krahn et al. (2001) (46)	12 mo	14 (52)	6 (20)	.012	• Crossover offered to patients with negative results • 1 of 6 switching to ELR was diagnosed and 8 of 13 switching to ILR was diagnosed (p=.07)

ECG: electrocardiography; ELR: external loop recorder; FU: follow-up; ILR: implantable loop recorder; mo: month(s); QOL: quality of life; RCT: randomized controlled trial; [a]: mean.

Observational Studies

Multiple observational studies compared the diagnostic yield of ICMs to the HM and reported high rates of arrhythmia detection. (50-55) Several observational studies reported management outcomes following diagnoses, such as anticoagulation initiation or cardiac procedures. (56-59)

Safety of ILRs

Mittal et al. (2015) reported on safety outcomes related to the use of an ILR, based on data from 2 studies, the Reveal® LINQ Usability study and the Reveal® LINQ Registry. (60) The Usability study enrolled 151 patients at 16 European and Australian centers; adverse events were reported for the first month of follow-up. The Registry is a multicenter post-marketing surveillance registry, with a planned enrollment of at least 1200. At the time of analysis, 161 patients had been enrolled. For Registry patients, all adverse events were recorded when they occurred. The device is inserted with a preloaded insertion tool via a small skin incision. In the Usability study, 1 serious adverse event was recorded (insertion site pain); in the Registry study, 2 serious adverse events were recorded (1 case each of insertion site pain and insertion site infection). The rates of infection and procedure-related serious adverse events in the Usability study were 1.3% and 0.7%, respectively, and 1.6% and 1.6%, respectively, in the Registry study.

Section Summary: Implantable Loop Recorders (ILRs)

Several RCTs have reported high rates of arrhythmia detection with the use of ILRs compared

with external event monitoring or Holter monitoring. These studies support the use of a progression in diagnostics from an external event monitor to ILR when longer monitoring is needed. Some available trials evaluating the detection of AF after ablation procedures or in patients with cryptogenic stroke used ILRs as an initial ambulatory monitoring strategy, after a negative HM. Many observational studies reported the initiation of treatment (for example, anticoagulation therapy or pacemaker implantation) following the confirmation of diagnoses with the ILR. Because these treatments are known to be effective, it can be concluded that long-term monitoring with ILRs will improve health outcomes.

IMPLANTABLE CONTINUOUS INTRACARDIAC ISCHEMIA MONITORING

According to the National Institutes of Health (NIH), continuous monitoring of the culprit artery is mandatory to determine the correct therapeutic intervention. While coronary angiography reveals vessel anatomy, it is only for a brief moment, and intracardiac ischemia detection or monitoring system (IIDS) monitors may be limited in the arrhythmia captured, based on the type of system used and/or inability to analyze acute ischemic events (ST-segment shifts/ST-shifts), and patient compliance. The NIH included a current perspective and future direction review of silent myocardial infarction (MI) that stated, "The goal of therapeutic intervention is to reverse ongoing ischemia and to interrupt or prevent myocardial cell death." (61) The authors deduce that to get to therapeutic goal, use of implantable monitoring is one solution.

The AngelMed® Guardian™ System is a permanent implantable continuous IIDS, also known as an implantable cardiac monitor with patient alert. In the approval of the IIDS or AngelMed® Guardian™ System by the U.S. Food and Drug Administration (FDA), 6 studies were reviewed, as the basis of the criteria used to make appropriate patient selection. (62, 63)

<u>Studies Reviewed by the FDA</u>

The clinical trials used by the FDA included observational studies, RCTs, and case series; all will be summarized below:

- In 2005, Fischell et al. reported the first clinical investigation examining the ability of an intracardiac right ventricular (RV) electrode to identify the early onset of myocardial ischemia or injury. (64) The patient health benefit was the alert process to them when there was a heart rhythm variance. This observational study of 14 patients with 17 lesions appeared to demonstrate the ability of the RV implanted lead, detecting the myocardial injury during a balloon angioplasty procedure. The study established the correct protocol evaluating cardiac injury and instructions for patients being monitored.
- Day and Young, in 2012, reviewed 3 clinical studies confirming that subcutaneous vibrotactile alarms showed the greatest potential in alerting a patient to take steps urgently to seek medical care. (65) The first study included 20 patients. Implantation was not done. The study was solely to identify the response to visual and auditory alarms. The low-priority alarms did not evoke the same level of response as the high-priority alarms. Each patient did identify and categorize the low- versus high-priority patterns. The second study evaluated what the patient would do when the alarm occurred. After training and 6 weeks later, 95% of the participants correctly answered how they would respond to an alarm. An interesting conclusion, respondents differed significantly in motivation from "real" patients

experiencing a heart condition. The respondents did not have a life-threatening diagnosis. The final study included 17 patients with high-risk for a MI. Data was collected following alarm training, and at 1-, 3-, and 6-month follow-up visits. All patients were taught how to respond to vibrotactile, auditory, and visual ques. At each of the follow-up visits, patients were tested on varying alarms, frequency and intensity. All but 1 patient of the 17 correctly identified the alarms.

- In 2010, Fischell et al. described results of intracardiac monitoring in 37 patients at high-risk for acute coronary syndromes. (66) The implanted monitor continuously evaluated the patients' ST-segments sensed from a conventional pacemaker RV apical lead, alerting patients to a detected ischemic event. During the follow-up, 4 patients experienced ST-segment changes, in the absence of an elevated heart rate. The median alarm-to-door was 19.5 minutes. Treatment included hospital monitoring, leading to angiogram and/or intravascular ultrasonography, which confirmed thrombotic coronary occlusion/rupture plaque. Of note, there were 2 false positive alarms related to arrhythmias, and 1 alarm due to a programing error. The alert-to-door, using this intracardiac monitoring, response time was far shorter than the typical patient at high-risk of recurrent coronary syndromes presenting for evaluation with 2- to 3-hour delays.
- A phase 2 pivotal trial, reported in 2009 by Hopenfeld et al., of 55 participants, in both the U.S. and Brazil, had the AngelMed® Guardian™ implanted to detect acute ischemic events. (67) When the ST-segment shift was greater than programmed heart-rate dependent threshold, the device would generate an emergency alarm. Partial results demonstrated that the intracardiac ECG was nearly noise-free and detection of the ST-shift was effective.
- Gibson et al. (2012) described the first 76 patients in the U.S. and Brazil CARDIOSAVER study who were diagnosed with high-risk coronary artery disease (CAD). (68) Monitors were implanted in all 76 patients. During the follow-up of 187.2 patient-years, emergency alarms occurred for recurrent events confirmed occlusions. Mean durations of the ST-shifts were 56 and 78 minutes, with 9 emergency alarms last less than 5 minutes. The size and duration of the ST-shifts changes did not correspond to the severity of the events as measured using conventional tests. The authors concluded that continuous intracardiac monitoring in high-risk acute coronary syndrome (ACS) patients provided a unique clinical perspective that ST-segment changes are rare events and even short-lived changes can reflect in medically relevant episodes of ischemia.
- In the FDA's Summary of Safety and Effectiveness Data (SSED) document, the CARDIOSAVER study published in Brazil only, was summarized "the CARDIOSAVER study was designed to better understand the proper functioning of the [AngelMed®] Guardian system as it responds to an occlusion of a human coronary artery. (63) The study included 20 subjects at high-risk for heart attack, with the added indications that they had: 1) demonstrated ischemia on an exercise stress test; 2) had an angiogram showing a stenosed coronary artery; and 3) had a clinical indication for angioplasty and/or stenting. After the implantation and balloon occlusion studies were completed, CARDIOSAVER subjects were sent home with daily ambulatory monitoring and alerting activated, and additional spontaneous coronary occlusive events were then detected. The results of this study included data providing the first human examples of Guardian alerting for real-life ischemic events that were caused by vulnerable plaque rupture in a coronary artery. These data were

convincing and showed the potential of the implanted AngelMed® Guardian™ to detect acute coronary occlusion in subjects to enable potentially life or heart muscle-saving early coronary intervention/revascularization."

- A STEMI (ST Elevation Myocardial Infarction) trial from Gibson et al. (2014) reported on the rationale and design of the AngelMed® Guardian™ in a randomized, prospective clinical investigation. (69) Patients with either high-risk post-ACS or previous multivessel coronary artery bypass graft (CABG) surgery were implanted with the monitoring device. The patients were randomized to have the alerting feature turned on versus turned off for the first 6 months. Patients returned at the 1-, 3-, and 6-month follow-up, then every 6-month follow-up visits or until closure of the investigational device exemption (IDE) was completed. The goal of this study was to reduce the time from the alert to presentation at a medical facility. The median time from detection or arrival to the medical facility was 51 minutes for the patients with the alarm turned on. For those in the control group, without the alarm, the median time was over 30 hours. The control patients did have the ST-shift recorded; despite the fact the alarm was turned off.

In 2016, Rogers et al. published an overview of the 2016 US Food and Drug Administration Circulatory System Devices Panel Meeting on the AngelMed Guardian System. (85) This meeting was to consider a PMA application of the AngelMed Guardian System based on the results of the pivotal ALERTS trial (NCT00781118). The panel clarified that the device should be considered only in high-risk patients, because this was the population studied in the ALERTS trial. The panel was doubtful that a secondary end point should be used in the proposed indications because the primary effectiveness end point was not met. Postapproval plans including a physician education program and prospective registry were considered acceptable. Many members of the panel recognized the unmet clinical need for devices to improve recognition of silent acute myocardial infarctions, expressing both enthusiasm for the AngelMed technology and concern over the results of the ALERTS trial. After careful deliberations, the panel voted:

a. Concerning the safety of the AngelMed Guardian System, the panel voted against (4:8). Panel members highlighted that the risks of the device were not just those of the implantation, but also the risks of additional tests triggered by false-positive alerts.
b. Concerning the effectiveness of the AngelMed Guardian System, the panel voted unanimously against (0:12) accepting the effectiveness data presented by the Sponsor, citing concerns with trial conduct and statistical analysis and the high number of patients with ACS events that were not recognized by the device.
c. The panel voted unanimously (0:12) that the benefits of the AngelMed Guardian System did not outweigh the risks and therefore recommended against approving the premarket approval application.

Gibson et al. (2019) reported on the ALERTS trial that was conducted to determine the safety and efficacy of the AngelMed Guardian system. (70) The trial was a prospective, randomized multicenter trial that used a Bayesian adaptive design to analyze sample size of patients based on interim treatment effect. Patients were selected based on high-risk status with a prior

history of coronary artery disease, with 97% having had previous revascularization. A total of 910 patients were implanted with the Guardian device, with 451 in the treatment arm (device on) and 456 in the control arm in which the device was deactivated. After the 6-month randomized period, the alarms in all devices were activated. The primary endpoints of the trial were the proportion of patients free from system-related complications and a composite effectiveness endpoint of late arrival (>2 hours) after a confirmed occlusive event, new Q-wave, and cardiac or unexplained death. The primary safety endpoint was met with a 96.7% event-free rate. The primary effectiveness endpoint was not met. The posterior probability of event reduction didn't meet the threshold for statistical significance and multiple study conduct issues were observed, especially with respect to the time-to-door and the new Q wave MI endpoints. The quality of the electrocardiogram data and the inconsistency of the Q wave results caused early termination of the trial.

Section Summary: Implantable Continuous Intracardiac Ischemia (IIDS) Monitoring
The studies utilized by the FDA to issue the premarket approval process (PMA) for the AngelMed® Guardian™ are small observational/case series, not including the 1 randomized trial. Additionally, the FDA panel members voted unanimously against the system based off the ALERTS clinical trial results. The panel clarified that the device should be considered only in high-risk patients, because this was the population studied in the ALERTS trial. These few studies have confirmed the responses by patients to the auditory, visual, and tactile alarms, reaction times from alert-to-door, capturing true ST-shifts indicating thrombotic coronary occlusion/rupture plaque in patients with high-risk ACS. Response times to seek medical treatment were reduced when compared to patients without the alarm. Additional studies are needed to confirm outcomes described in the smaller studies to capture arrhythmic changes and alerting the patient to seek medical evaluation.

ECRI Reviews
In March 2019 (updated January 2022), ECRI completed 2 reviews. This first was a Hotline Response on "Outpatient Cardiac Telemetry Monitors for Diagnosing and Managing Cardiac Arrhythmias", with their focus on clinical utility. (71) Their conclusion was inconclusive because of the limitations of data. ECRI based this conclusion on the following:
"Available studies indicate outpatient telemetry increases diagnostic yield (i.e., increases arrhythmia detection), but this is indirect evidence that does not necessarily translate to improved patient outcomes (i.e., clinical utility, such as reduced arrhythmia-related adverse events [AEs]). Variability in study methods and designs that are at high risk of bias also limits interpretation of findings and evidence-based conclusions. Clinical guidelines recommend outpatient monitoring for arrhythmia diagnosis and evaluation but leave the choice of monitoring modality to the clinician." This was based on:

- The clinical validity was "1 prospective diagnostic cohort study (n = 152) [Lauschke et al., 2017 (72)] reported 92% sensitivity for arrhythmia with the BioMonitor® implanted system compared with 48-hour Holter monitoring. 1 prospective study (n = 36) [Casteletti et al., 2018 (73)] reported low false-positive (3/132) and false-negative (10/219) long QT interval detection rates with BodyGuardian."
- The clinical utility was "no direct evidence regarding clinical utility—only indirect evidence

pertaining to diagnostic yield. 1 systematic review (SR) of 50 studies (Sposato et al. 2015 [23]) reported similar diagnostic yields for AF using CardioNet Mobile Cardiac Outpatient Telemetry (MCOT®) and event recorders after stroke, but 1 registry study (n = 78,490) [Derkac et al. 2017 (9)] reported higher yield with CardioNET in patients with suspected arrhythmia. 1 retrospective case series (n = 100) [Vanegas-Cadavid et al. 2018 (74)] detected arrhythmias in 22% of Holter-negative patients with the SEEQ™ monitor; 1 retrospective case series (n = 154) reported telemetry detected arrhythmias at a mean 4 months earlier than scheduled interrogation of implanted LINQ monitors."

ECRI concluded the evidence limitations as the following:
"The SR pertains only to patients with stroke, and findings were of unclear significance because of wide confidence intervals. A comparative study of registry data and 2 case series are at high risk of bias because of retrospective design; 2 diagnostic cohort studies are at high risk of bias because of small sample size and high patient attrition, respectively. Longitudinal studies reported on diagnostic yields and time to diagnosis, which are indirect measures of clinical utility that do not necessarily translate to improved patient outcomes."

The second ECRI review in March 2019 (updated September 2022) was a Product Brief on BioTel MCOT formerly CardioNet Ambulatory ECG Monitor (BioTelemetry, Inc.) for Diagnosing and Managing Cardiac Arrhythmias" focusing on the MCOT®, which updates providers regularly and alerts them of arrhythmia events. (75) Their conclusion was inconclusive because of the limitations of data. ECRI based this conclusion on the following:
"Available studies provide only indirect evidence (i.e., diagnostic yield) of MCOT's utility compared with that of other ambulatory monitors and do not inform whether MCOT use reduces arrhythmia-related adverse events (AEs). Variability in study methods and study designs at risk of bias also limit interpretation of diagnostic yield findings. Comparative studies that report on arrhythmia-related morbidity and mortality are needed to confirm MCOT's clinical utility, but none are ongoing."

In January 2020 (updated February 2022), ECRI published a product brief of the AngelMed Guardian system (Angel Medical System, Inc., Eatontown, NJ, USA) which is a fully implanted electrocardiography (ECG) device intended for continuous monitoring of patients with acute coronary syndrome (ACS) history and high recurrence risk. (76) Their evidence was inconclusive, and the conclusion noted the following:
"Evidence is too limited in quantity and quality to assess whether AngelMed cardiac monitoring benefits patients. Results from a randomized controlled trial (RCT) suggest that AngelMed alerts may help patients seek care promptly when alerted by the device; however, the RCT is at high risk of bias from serious protocol breaches. Moreover, AngelMed has potential to increase adverse event risks by leading some patients not to seek immediate care if an AngelMed alert does not accompany ACS symptoms. Large, multicenter RCTs that assess AngelMed's accuracy in patients with a history of ACS and report on diagnostic accuracy and patient-oriented outcomes at long-term follow-up (>5 years) are needed. One ongoing study may provide some additional evidence."

Summary of Evidence

Outpatient Cardiac Telemetry (OCT)

For individuals who have signs and/or symptoms suggestive of arrhythmia who receive outpatient cardiac telemetry (OCT), the evidence includes randomized controlled trials (RCTs) and nonrandomized studies evaluating rates of arrhythmia detection using OCT. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. The addition of real-time monitoring to outpatient ambulatory monitoring is considered an enhancement to existing technology. Because OCT is as good as ambulatory event monitors (AEMs) to detect atrial fibrillation (AF), the evidence does demonstrate a clinically significant incremental benefit for OCT. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Implantable Loop Recorders

For individuals who have cryptogenic stroke with a negative standard workup for atrial fibrillation (AF) who receive long-term ambulatory cardiac monitoring, the evidence includes systematic reviews of RCTs comparing AEM with standard care. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. RCTs evaluating a long-term AF monitoring strategy poststroke have reported significantly higher rates of AF detection with longer term ambulatory monitoring. The available evidence has suggested that long-term monitoring for AF after cryptogenic stroke is associated with improved outcomes, but the specific type of monitoring associated with the best outcomes is not established, because different long-term monitoring devices were used across the studies. Trials demonstrating improved outcomes have used event monitors or ILRs. In addition, there are individual patient considerations that may make 1 type of monitor preferable over another. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have signs and/or symptoms suggestive of arrhythmia with infrequent symptoms who receive patient- or auto-activated implantable ambulatory event monitoring, the evidence includes RCTs comparing implantable loop recorders with shorter term monitoring, usually 24- to 48-hour Holter monitoring. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. Studies assessing prolonged ILRs in patients have reported high rates of arrhythmia detection compared with shorter external event or Holter monitoring. These studies have supported use of a progression in diagnostics from an external event monitor to ILR when longer monitoring is needed. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Implantable Continuous Intracardiac Ischemia Detection or Monitoring System (IIDS)

For individuals at high-risk of having a myocardial infarction (MI), due to acute coronary syndrome (ACS) or bypass surgery (CABG), the evidence includes clinical trials reviewed by the U.S. Food and Drug Administration (FDA) for premarket approval of the technology. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. Studies assessed the placement of intracardiac implant, capture of ST-shifts, the types of alarms

to alert the patient, and response to seek medical care. The clinical trials were small, 1 randomized study and 1 randomized multicenter trial did not meet its pre-specified primary efficacy endpoint. Additional studies are needed to confirm overall survival and morbid events. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Clinical Practice Guidelines and Position Statements

American Academy of Neurology (AAN)

In 2014 (reaffirmed in 2022), the AAN updated its guidelines on the prevention of stroke in patients with nonvalvular atrial fibrillation (NVAF). (77) These guidelines made the following recommendations on the identification of patients with occult NVAF:

- "Clinicians might obtain outpatient cardiac rhythm studies in patients with cryptogenic stroke without known NVAF, to identify patients with occult NVAF (Level C).
- Clinicians might obtain cardiac rhythm studies for prolonged periods (e.g., for 1 or more weeks) instead of shorter periods (e.g., 24 hours) in patients with cryptogenic stroke without known NVAF, to increase the yield of identification of patients with occult NVAF (Level C)."

American Heart Association (AHA), American College of Cardiology (ACC), et al.

The ACC, the AHA, the American College of Clinical Pharmacy (ACCP), and the Heart Rhythm Society (HRS) (2023) updated guidelines initially issued in 2014 (4) on the management of patients with atrial fibrillation (AF). (78) These guidelines recommended the use of Holter or event monitoring if the diagnosis of the type of arrhythmia is in question, or as a means of evaluating rate control.

The ACC/AHA/HRS (2017) collaborated on guidelines on the evaluation and management of patients with syncope (79) and patients with ventricular arrhythmias. (80) Cardiac monitoring recommendations are summarized below in Tables 9 and 10.

Table 9. Cardiac Monitoring Recommendations, AHA/ACC/HRS

Recommendation	COR[a]	LOE[b]
Choice of a specific cardiac monitor should be determined on the basis of frequency and nature of syncope events. (79)	I	C-EO
To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, the following external cardiac monitoring approaches can be useful: Holter monitor, trans-telephonic monitor, external loop recorder, patch recorder, and outpatient cardiac telemetry. (79)	IIa	B-NR
To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, an implantable cardiac monitor can be useful. (79)	IIa	B-R
Ambulatory electrocardiographic monitoring is useful to evaluate whether symptoms including palpitations, presyncope, or syncope, are caused by VA. (80)	I	B-NR

In patients with cryptogenic stroke (i.e., stroke of unknown cause), in whom external ambulatory monitoring is inconclusive, implantation of a cardiac monitor (loop recorder) is reasonable to optimize detection of silent AF. (78)	IIa	B-R

ACC: American College of Cardiology; AF: atrial fibrillation; AHA: American Heart Association; COR: class of recommendation; HRS: Heart Rhythm Society; LOE: level of evidence; VA: ventricular arrhythmia.
[a] COR Definitions: I: strong recommendation; IIa: benefit probably exceeds risk (moderate).
[b] LOE Definitions: B-NR: moderate level based on well-executed nonrandomized studies; B-R: moderate level based on randomized trials; C-EO: consensus of expert opinion based on clinical experience.

Table 10. Patient Selection Recommendations for Outpatient Cardiac Telemetry or Implantable Cardiac Monitor, AHA/ACC/HRS

Type of Monitor	Patient Selection
Outpatient Cardiac Telemetry	• Spontaneous symptoms related to syncope and rhythm correlation. • High-risk patients needing real-time monitoring.
Implantable Cardiac Monitor	• Recurrent, infrequent, unexplained syncope.

ACC: American College of Cardiology; AHA: American Heart Association; HRS: Heart Rhythm Society.

In 2018, the ACC et al. released a guideline addressing the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay. (81) The guideline states, "External loop recorders, transtelephonic event recorders, adhesive patch recorders, and mobile continuous outpatient telemetry monitoring provide a higher diagnostic yield than 24- or 48-hour Holter monitoring because of the longer period of monitoring. These prolonged monitoring strategies can be useful in the evaluation of suspected bradycardia or conduction disorders… Choice of device is predicated on frequency of symptoms and the degree to which symptoms incapacitate the patient." The guideline recommends MCOT® for "spontaneous symptoms, potentially related to bradycardia or conduction disorder, that are too brief, too subtle, or too infrequent to be readily documented with patient activated monitors" and "in high-risk patients whose rhythm requires real-time monitoring."

International Society for Holter and Noninvasive Electrocardiology/Heart Rhythm Society
The International Society for Holter and Noninvasive Electrocardiology and the HRS (2017) issued a consensus statement on ambulatory electrocardiogram and external monitoring and telemetry. (82) Below are 2 summary tables from the consensus statement, detailing advantages and limitations of OCT and implantable ECG techniques (Table 11) and recommendations for the devices that are relevant to this medical policy (Tables 12).

Table 11. Advantages and Limitations of Ambulatory OCT Techniques, International Society for Holter and Noninvasive Electrocardiology/HRS

Monitoring Technique	Advantages	Limitations
OCT	• Multilead, so higher sensitivity and specificity of arrhythmia	• Long-term patient acceptance is reduced due to requirement of

	detection. • Streams data continuously; can be programmed to auto-detect and auto-send events at prescribed time intervals. • Immediate alarm generation on event without patient interaction.	daily electrode changes.

OCT: outpatient cardiac telemetry; HRS: Heart Rhythm Society.

Table 12. Select Condition Recommendations for Use of Telemetry as an AEM, International Society for Holter and Noninvasive Electrocardiology/HRS

Recommendation	COR[a]	LOE[b]
Unexplained syncope, when tachycardia suspected	I	B-R
Unexplained palpitation	I	B-R
Detection of atrial fibrillation, triggering arrhythmias, and post-conversion pauses	IIa	B-NR
Cryptogenic stroke, to detect undiagnosed atrial fibrillation	I	B-R

AEM: ambulatory event monitor; COR: class of recommendation; LOE: level of evidence; HRS: Heart Rhythm Society.

[a] COR Definitions: I, strong recommendation; IIa: benefit probably exceeds risk.

[b] LOE Definitions: B-NR, moderate level based on well-executed nonrandomized studies; B-R: moderate level based on randomized trials.

United States (U.S.) Preventive Services Task Force Recommendations

In 2022, the U.S. Preventive Services Task Force updated its recommendation on Screening for Atrial Fibrillation and concluded, "For adults 50 years or older who do not have signs or symptoms of atrial fibrillation: The current evidence is insufficient to assess the balance of benefits and harms of screening for AF (Grade: I statement)." (83)

Medicare National Coverage

The Centers for Medicare & Medicaid Services (2004) implemented a national coverage determination (NCD) for electrocardiographic services. (84) This NCD includes descriptions of the Holter monitor and event recorders (both external loop recorders and implantable loop recorders). Ambulatory cardiac monitors are covered when there is documentation of medical necessity. Indications for use include detection of symptomatic transient arrhythmias and determination of arrhythmic drug therapy (to either initiate, revise, or discontinue the therapy).

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in Table 13.

Table 13. Summary of Key Trials

NCT Number	Trial Name	Planned	Completion

		Enrollment	Date
Ongoing			
NCT05957315	Mobile Cardiac Outpatient Telemetry for Unexplained Syncope: Time to Treatment, Arrhythmia Diagnosis and Outcome	160	Oct 2025
NCT04371055	Intensive Heart Rhythm Monitoring to Decrease Ischemic Stroke and Systemic Embolism - the Find-AF 2 Study	5200	Dec 2026
NCT03940066	Evaluation of Ambulatory Monitoring of Patients After High-risk Acute Coronary Syndrome Using Two Different Systems: Biomonitor-2 and Kardia Mobile (Monitor-ACS)	169	Jun 2023 (active, not recruiting)
Unpublished			
NCT04126486[a]	A Study to Determine if Identification of Undiagnosed Atrial Fibrillation in People at Least 70 Years of Age Reduces the Risk of Stroke (GUARD-AF)	11,931	Jun 2023
NCT02786940	Remote Cardiac Monitoring of Higher-Risk Emergency Department Syncope Patients after Discharge - A Pilot Study (REMOSYNC)	99	Mar 2020
NCT03541616	Prevalence of Subclinical Atrial Fibrillation in Heart Failure Patients and Its Relationship With Hospital Readmission (PROTECT-HF)	242	Mar 2023
NCT03072693	Daily Ambulatory Remote Monitoring System for Post-Discharge Management of Acute Decompensated Heart Failure	876	Apr 2023 (unknown status)
NCT04306978	Impact of the CareLink Express Remote Monitoring System on Early Detection of Atrial Fibrillation	200	Jan 2023 (unknown status)

NCT: National Clinical Trial.

[a] denotes industry involvement.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	33285, 33286, 93228, 93229, 93297, 93298, 93799, 99091, 0525T, 0526T, 0527T, 0528T, 0529T, 0530T, 0531T, 0532T, 0650T
HCPCS Codes	C1764, C1833, E0616, [Deleted 12/31/2023: G2066]

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
01/01/2025	Document updated with literature review. Coverage unchanged. References 78 and 85 added.
09/15/2023	Document updated with literature review. The following changes were made to the Coverage Section: 1) To Note 1 wording was changed from "DOES NOT ADDRESS" to "DOES NOT FOCUS on." 2) For outpatient cardiac telemetry medically necessary monitoring of a suspected atrial fibrillation arrhythmia was changed from: following a non-diagnostic AEM for at least 30 days to "a noninvasive ambulatory cardiac monitoring of not less than 14 continuous days is inconclusive or non-diagnostic (e.g., patch monitors, external event monitors)." 3) For implantable cardiac rhythm event monitors in the small subset of patients who experience recurrent symptoms so infrequently that a prior trial of an external AEM for at least 30 days without a symptom has been unsuccessful to "small subset of individuals who experience recurrent symptoms so infrequently that a prior trial of a noninvasive ambulatory cardiac monitoring of not less than 14 continuous days without a symptom is inconclusive or non-diagnostic (e.g., patch monitors, external event monitors). References 31, 34, 35, 61, and 83 added; some updated and others removed.
01/15/2023	Reviewed. No changes.

08/15/2021	Document updated with literature review. The following change was made to the Coverage section: Transthoracic echocardiography (TTE) was added to the statement for the use of implantable cardiac rhythm/implantable loop recorders (ILRs) event monitors in patients who are ≥ 40 years of age and require long-term monitoring for cryptogenic stroke. No new references added; some updated and others removed.
01/01/2021	Document updated with literature review. The following changes were made to the Coverage section: Zio XT was added to NOTE 1 for clarification of the Zio Patch, and Zio AT ECG Monitoring System was added as an additional example of the outpatient cardiac telemetry/mobile cardiac telemetry systems. References 67 and 73 were added and others updated.
01/01/2020	Document updated with literature review. The following coverage change was made for outpatient cardiac telemetry, from not medically necessary to medically necessary when meeting specific criteria. The following criteria was added to the "including but not limited to" experimental, investigational and/or unproven statement regarding other uses of implantable cardiac rhythm event monitors, including any form of cardiac telemetry: "Monitoring asymptomatic patients with risk factors for arrhythmias." The title was changed from Implantable Cardiac Rhythm Event Monitors and Outpatient Cardiac Telemetry. References 7, 9, 18, 19, 39, 47-49, 51, 61-77, 79, and 82 added; several reorganized or removed.
08/15/2017	Reviewed. No changes.
01/01/2017	Document coverage changed: 1) Removed patient-activated or auto-activated external ambulatory event monitors; 2) Removed continuous ambulatory monitors that record and store information for periods longer than 48-hours (e.g., Zio® Patch system). Title changed from "Ambulatory Event Monitors and Outpatient Cardiac Telemetry" to "Implantable Cardiac Rhythm Event Monitors and Outpatient Cardiac Telemetry."
09/15/2016	Document updated with literature review. The following was added to the medically necessary coverage statement for external ambulatory event monitors, "continuous ambulatory monitors that record and store information for periods longer than 48 hours." The following was added to the medically necessary coverage statement for internal ambulatory event monitors, "In patients who require long-term monitoring for AF or possible AF or In patients who are ≥ 40 years of age and require long-term monitoring for cryptogenic stroke when meeting ALL the following tests, evaluated by a neurologist, have established the diagnosis of a prior cryptogenic ischemic stroke" when specific criteria has been met for cryptogenic ischemic stroke only.
07/15/2015	Document updated with literature review. The following criteria statement was added to the use of patient-activated or auto-activated external ambulatory event monitors as may be considered medically necessary: Patients was cryptogenic stroke who have a negative standard work-up from

	atrial fibrillation (AF) including a 24-hour Holter monitor. The following was added to the use of implantable ambulatory event monitors as may be considered medically necessary: in the small subset of patients who experience recurrent symptoms so infrequently that a prior trial of external ambulatory event monitor for at least 30 days without a symptomatic has been unsuccessful. The following was changed from experimental, investigational and/or unproven: Continuous ambulatory monitors that record and store information for periods longer than 48-hours (e.g., Zio® Patch system) may be considered medical necessary as a diagnostic alternative to Holter monitoring or patient-activated or autoactivated external ambulatory event monitors in the following situations: Patients who experience infrequent symptoms (less frequently than every 48 hours) suggestive of cardiac arrhythmias (i.e., palpitations, dizziness, presyncope, or syncope); Patients with atrial fibrillation (AF) who have been treated with catheter ablation, and in whom discontinuation of systemic coagulation is being considered; Patients with cryptogenic stroke who have a negative standard work-up for AF including a 24-hour Holter monitor. Otherwise, coverage remains unchanged. Rationale and References revised and reorganized. Title was changed from Ambulatory Event Monitors and Mobile Outpatient Cardiac Telemetry.
11/15/2014	Document updated with literature review. The following was removed: 1) Coverage statement for Holter monitors (HMs). The following changes were made: 1) The use of patient-activated or auto-activated external ambulatory event monitors (AEMs) may be considered medically necessary as a diagnostic approach in patients with atrial fibrillation (AF) who have been treated with catheter ablation, and in whom discontinuation of systemic anticoagulation is being considered; 2) Real time, continuous outpatient cardiac telemetry is considered not medically necessary as a diagnostic alternative to AEMs; 3) Continuous ambulatory monitors that record and store information for periods longer than 48-hours (e.g., Zio® Patch system) are considered experimental, investigational and/or unproven; 4) Outpatient cardiac telemetry (e.g., mobile cardiac outpatient telemetry system by CardioNet®, HEARTLink II™, etc.) is considered not medically necessary because the clinical outcomes have not demonstrated this service as superior to, or more effective than less costly established ambulatory event monitor alternatives, such as autotrigger devices, according to published literature; and, 5) Other uses of ambulatory event monitors are considered experimental, investigational and/or unproven, including but not limited to: monitoring effectiveness of antiarrhythmic medications, for patients with cryptogenic stroke, detection of myocardial ischemia by detecting ST segment changes. The title changed from Ambulatory Cardiac Event Monitors (AEMs or CEMs) including Mobile Cardiac Outpatient Telemetry (MCOT). Description and Rationale reordered and significantly revised.

07/01/2012	The following change was made to Coverage: 1) The use of an EKG monitor patch system to evaluate heart rate measurements and rhythm analysis in asymptomatic or in patients who have experienced symptoms or events suggestive of cardiac arrhythmias, from 48-hours to up to 14-days, is considered not medically necessary. 2) The use of permanent implantable continuous intracardiac ischemia detection or monitoring system (IIDS) is considered experimental, investigational and unproven. CPT/HCPCS codes updated.
05/01/2009	CPT/HCPCS code(s) updated
11/01/2008	Revised/updated entire document. This policy is no longer scheduled for routine literature review and update.
06/15/2007	Rationale revised
07/15/2006	New medical document originating from position statement
04/01/2006	New medical document originating from position statement
04/01/2004	Revised/updated entire document
02/01/2002	New medical document originating from position statement
03/01/2000	Revised/updated entire document
01/01/2000	CPT/HCPCS code(s) updated
09/01/1999	Revised/updated entire document
05/01/1996	Medical policy number changed
10/01/1995	Revised/updated entire document
07/01/1994	Revised/updated entire document
10/01/1993	Revised/updated entire document
04/01/1993	Revised/updated entire document
10/01/1992	Revised/updated entire document
01/01/1992	Revised/updated entire document
09/01/1991	New medical document