BlueCross BlueShield of Alabama

Name of Policy:

Ambulatory Event Monitors and Mobile Cardiac Outpatient Telemetry

Policy #: 356
Category: Medical

Latest Review Date: May 2018
Policy Grade: B

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

There are a wide variety of devices available for outpatient cardiac rhythm monitoring. The primary purpose of these devices is the evaluation of suspected arrhythmias that have not been detected by office- or hospital-based 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 delivery of the information from patient to clinician. These devices may be used for the evaluation of symptoms suggestive of arrhythmias, such as syncope or palpitations, but also may be used in the detection of 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 for the purpose of detecting 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. In addition, ambulatory cardiac monitoring may be used for evaluation of paroxysmal atrial fibrillation (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 review, but some general principles on the use of ambulatory monitoring are discussed.

Arrhythmias are an important potential cause of syncope or near-syncope, which may in some cases be described as dizziness. An ECG is generally indicated whenever there is suspicion of a cardiac cause of syncope. Some arrhythmic causes will be apparent on ECG. However, in patients in whom an ECG is not diagnostic, longer monitoring may be indicated. The 2009 guidelines from the European Society of Cardiology suggest that in individuals with clinical or ECG features suggesting an arrhythmic syncope, ECG monitoring is indicated; they also state that the "duration (and technology) of monitoring should be selected according to the risk and the predicted recurrence rate of syncope." Similarly, guidelines from the National Institute for Health and Care Excellence (2014) 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. The Holter monitor is recommended if transient loss of consciousness occurs several times a week. If the frequency of transient loss of consciousness is every one to two weeks, an external event recorder is recommended; and if the frequency is less than once every two 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 2011 position paper from the European Heart Rhythm Association indicates 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.

Atrial Fibrillation (AF) 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, direct cardioversion, catheter-based radiofrequency- or cryo-energy-based ablation, or one of several surgical techniques, depending on the patient's comorbidities and associated symptoms.

AF is associated with the development of thrombi in the atria, often the left atrial appendage. Patients with AF are at risk for ischemic stroke due to the risk of embolism of the thrombus. 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 and American College of Cardiology guidelines for patients with a history of stroke or transient ischemic attack.

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.

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. Paroxysmal AF confers an elevated risk of stroke, just as persistent and permanent AF do. 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 allows for the evaluation of cardiac electrical activity over time, in contrast to a static electrocardiogram (ECG), which only permits the detection of abnormalities in cardiac electrical activity at a single 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 up to about 24 to 72 hours. Traditionally, most Holter monitors had 3 channels based on 3 ECG leads. However, some currently available Holter monitors have up to 12 channels. Holter monitors are an accepted intervention in a variety of settings where a short period (24-48 hours) of comprehensive cardiac rhythm assessment is needed (e.g., suspected arrhythmias when symptoms [syncope, palpitations] are occurring daily). These devices are not the focus of this review.

Various classes of devices are available for situations where longer monitoring than can be obtained with a traditional Holter monitor is needed. Because there may be many devices within each category, a comprehensive description of each device is beyond our scope. Specific devices

may 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

Device Class	Description	Example Devices
Noncontinuous devices with memory (event recorder)	Devices not worn continuously but rather activated by patient and applied to skin in the precordial area when symptoms develop	• Zio® Event Card (iRhythm Technologies, San Francisco, CA) • REKA E100™ (REKA Health, Bridgewater, NJ)
Continuous recording devices with longer recording periods	Devices continuously worn and continuously record via ≥1 cardiac leads and store data for a longer period than traditional Holter (14 d)	• Zio® Patch system (iRhythm Technologies, San Francisco, CA)
External memory loop devices (patient- or autotriggered)	Devices continuously worn and continuously store a single channel of ECG data in a refreshed memory. If device is activated, the ECG is then recorded from the memory loop for the preceding 30-90 s and for next minute or so. These devices may be activated by a patient when symptoms occur (patient-triggered) or by an automated algorithm when changes suggestive of an arrhythmia are detected (autotriggered).	• Patient-triggered: Explorer™ Looping Monitor (LifeWatch Services, Switzerland) • Autotriggered: LifeStar AF Express™ Auto-Detect Looping Monitor (LifeWatch Services, Switzerland) • Autotriggered or patient-triggered: King of Hearts Express® AF (Card Guard Scientific Survival, Rehovot, Israel)
Implantable memory loop devices (patient- or autotriggered)	Devices similar in design to external memory loop devices but implanted under the skin in the precordial region	• Autotriggered: Reveal® XT ICM (Medtronic, Minneapolis, MN) • Autotriggered: BioMonitor, Biotronik SE (Berlin, Germany)
Mobile cardiac outpatient telemetry	Continuously recording or autotriggered memory loop devices that transmit data to a central recording station with real-time monitoring and analysis	• CardioNet MCOT (BioTelemetry, Malvern, PA) • LifeStar Mobile Cardiac Telemetry (LifeWatch Services, Switzerland) • SEEQ Mobile Cardiac Telemetry (Medtronic, Minneapolis, MN)

ECG: electrocardiogram

There are also devices that combine features of multiple classes. For example, the LifeStar ACT Ex Holter (LifeWatch Services, Switzerland) is a 3-channel Holter monitor, 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, Houston, TX) is an external autotriggered memory loop device that can be converted to a real-time monitoring system. The eCardio Verité™ system (eCardio, Houston, TX) can be changed between a patient-activated event monitor and a continuous telemetry monitor. The Spiderflash-T (LivaNova, London, England) is an example of an external autotriggered or patient-triggered loop recorder, but, like the ZioPatch, can record 2 channels for 14 to 40 days.

Policy:

Effective for dates of service on and after March 20, 2017:

The use of **patient-activated or auto-activated external ambulatory event monitors OR continuous ambulatory monitors** that record and store information for periods longer than 48 hours **meets** Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a diagnostic alternative to Holter monitoring 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); **OR**
- Patients with atrial fibrillation who have been treated with catheter ablation, and in whom discontinuation of systemic anticoagulation is being considered; **OR**
- Patients with cryptogenic stroke who have a negative standard work-up for atrial fibrillation including a 24-hour Holter monitor.

The use of **implantable ambulatory event monitors, either patient-activated or auto-activated, meets** Blue Cross and Blue Shield of Alabama's medical criteria for coverage **the following situations:**

- In the small subset of patients who experience recurrent symptoms so infrequently that a prior trial of other external ambulatory event monitors has been unsuccessful; **OR**
- In patients with cryptogenic stroke who have had a negative standard work-up for atrial fibrillation including a 24-hour Holter monitor; **OR**
- For the evaluation of atrial fibrillation after an ablation procedure

The use of **outpatient cardiac telemetry (also known as mobile cardiac outpatient telemetry or MCOT) does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a diagnostic alternative to ambulatory event monitors in patients who experience infrequent symptoms (less frequently than every 48 hours) suggestive of cardiac arrhythmias (i.e., palpitations, dizziness, presyncope, or syncope) and is considered **investigational**.

O**ther uses of ambulatory event monitors (including outpatient cardiac telemetry) and mobile applications,** including but not limited to monitoring asymptomatic patients with risk factors for arrhythmia, monitoring effectiveness of antiarrhythmic medications and detection of myocardial ischemia by detecting ST- segment changes **do not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational**.

For Holter monitors, please refer to MP*# 461- Holter Monitoring (Ambulatory Electrocardiography)*

Effective for dates of service on or after June 1, 2015 and prior to March 20, 2017:

The use of patient-activated or auto-activated external ambulatory event monitors meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a diagnostic alternative to Holter monitoring in **any** of 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); **OR**
- Patients with **atrial fibrillation who have been treated with catheter ablation, and in whom discontinuation of systemic anticoagulation is being considered; OR**
- Patients with **cryptogenic stroke who have a negative standard work-up for atrial fibrillation including a 24-hour Holter monitor**.

The use of **implantable ambulatory event monitors, either patient-activated or auto-activated, meets** Blue Cross and Blue Shield of Alabama's medical criteria for coverage **in either of the following situations:**

- In the small subset of patients who experience **recurrent symptoms** so infrequently that a prior trial of **other external ambulatory event monitors has been unsuccessful, OR**
- In patients with **cryptogenic stroke who have had a negative standard work-up for atrial fibrillation including a 24-hour Holter monitor.**

Other uses of ambulatory event monitors, including outpatient cardiac telemetry, do not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and are considered investigational, **including but not limited to monitoring effectiveness of antiarrhythmic medications, and detection of myocardial ischemia by detecting ST segment changes.**

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent review covers the period through March 5, 2018. The following is a summary of the key literature to date.

Evidence reviews assess the clinical evidence to determine whether the use of a 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 to 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, two domains are examined: the relevance and the quality and credibility. To be

relevant, studies must represent one 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 is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials 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 review is structured around 3 questions: First, in what clinical situations, and with what classes of ambulatory event monitors (AEMs), do AEMs improve health outcomes? Second, under what circumstances are implantable AEMs associated with improved outcomes? Third, under what circumstances is real-time monitoring associated with improved outcomes?

For some of AEMs discussed in this evidence review, including monitors 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.

Ambulatory Event Monitors in the Detection of Arrhythmias

The following four subsections focuses on the clinical situations for which the use of AEMs is associated with improved health outcomes. Two clinical situations are considered. First, the use of AEMs in the diagnosis of cardiac rhythm abnormalities in individuals with signs and/or symptoms of arrhythmias (e.g., dizziness, syncope or near syncope, palpitations) is discussed. Specific arrhythmias may be relatively nonspecific in terms of the symptoms they cause. However, the diagnosis of some arrhythmias has well-defined management implications that are known to improve outcomes, such as the use of an implantable cardioverter defibrillator (ICD) in individuals with potentially lethal arrhythmias, or antiarrhythmic drugs or pulmonary vein isolation for the treatment of atrial fibrillation (AF). Therefore, identification of an arrhythmia is considered a reasonable end point in this case.

The second clinical situation relates to the use of AEMs in the detection of AF in specific clinical situations for which management may be changed based on AF detection. For example, if AF is not detected following catheter ablation, antiarrhythmic drugs may be discontinued. Another example is in the identification of AF following cryptogenic stroke.

Diagnosis of Suspected Arrhythmias in Symptomatic Patients

The diagnostic yield of monitoring with external event monitors depends on the underlying population, the inherent sensitivity of the device, and the duration of monitoring. External loop recorders have an established role in current clinical practice in evaluating suspected arrhythmias. A few pieces of evidence suggest that autotriggered event monitors have an inherent higher yield than patient-activated AEMs. Several studies, including an analysis of a database of 100,000 patients, compared the diagnostic yield of automatic and patient-activated arrhythmia recordings and reported an improved yield with autotriggering devices.

Hoefman et al (2010) published a systematic review on diagnostic tools for detecting cardiac arrhythmias. The literature search, conducted through March 2007, identified 28 studies for inclusion; 12 were single-arm studies and 16 were comparative studies. A meta-analysis was not possible due to the heterogeneity of the study populations and the devices tested. This review included studies of patients presenting with palpitations, and compared the yield of remote monitoring for several classes of devices: Holter monitors; patient-activated event recorders; autotriggered event recorders; and implantable loop recorders. The yield varied among devices, with the autotriggered devices offering the highest range of detection (72-80%), followed by the patient-activated devices (17%-75%), and Holter monitors (33-35%).

Continuous Monitors with Longer Recording Periods
Newer devices are available that record cardiac rhythms continuously, but for longer periods of time than traditional Holter monitors. For example, the Zio® Patch continuously records and stores information for up to two weeks. In addition to recording information for longer periods of time, this device uses "near-field" recording electrodes that differ from most other devices.

Several studies have evaluated the diagnostic yield of continuous monitoring for greater than 48 hours, either directly through comparison to Holter monitoring or indirectly through determination of the proportion of arrhythmias detected in the first 48 hours of monitoring.

Tuakhia et al (2013) published a study in 2013 evaluating the diagnostic yield of the Zio Patch. Data from the manufacturer was used to identify 26,751 first-time users of the device. The most common clinical indications were palpitations (40.3%), atrial fibrillation (AF) (24.3%), and syncope (15.1%). The mean duration of use was 7.6±3.6 days, and 95.9% of patients wore the device for more than 48 hours. At least one episode of arrhythmia was detected in 16,142 patients (60.3%). The authors compared the detection rate in the first 48 hours with the detection rate over the entire time period that the device was worn, with 70.1% of patients having their arrhythmia detected within the first 48 hours and 29.9% having their first arrhythmia detected after the first 48 hours. The overall yield was significantly higher when comparing the total monitored period with the first 48 hours (62.2% vs 43.9%, $p<0.001$). These data confirm previous studies that have shown that a substantial proportion of arrhythmias in symptomatic patients can be detected with a 48-hour period of monitoring and that longer monitoring periods increase the detection rate.

Barrett et al (2014) published a comparison of arrhythmia detection rates in 146 patients who underwent simultaneous monitoring with a 24-hour Holter monitor and a 14-day Zio Patch monitor. Included were patients referred for evaluation of a suspected cardiac arrhythmia at a single institution for the detection of atrioventricular block, pause, polymorphic ventricular tachycardia, supraventricular tachycardia, or AF. Holter monitoring detected 61 arrhythmias, while the Zio Patch detected 96 ($p<0.001$). Over the course of the monitoring period, 60 arrhythmias were detected by both devices, with 36 detected by the Zio Patch that were not detected by Holter monitoring and one detected by the Holter that was not detected by the Zio Patch. The investigators conducted within-subject comparisons of arrhythmia detection for the 24-hour period during which both devices were worn. Holter monitoring detected 61 arrhythmia events, compared with 52 detected by the Zio Patch ($p=0.013$). This study further suggests that

extended monitoring may increase the diagnostic yield of cardiac monitoring. However, a relatively large number of missed events occurred with the Zio Patch during the period of simultaneous monitoring, which may have clinical significance if its performance is similar in non-research settings.

In 2015, Bolourchi et al evaluated the diagnostic yield of 14 days of monitoring with the Zio Patch in a cross-sectional study of 3,209 children who were included in a manufacturer registry. Patients' age ranged from one month to 17 years. Indications for monitoring included palpitations (n=1138 [95.5%]), syncope (n=450 [14.0%]), unspecified tachycardia (n=291 [9.1%]), paroxysmal supraventricular tachycardia (SVT) (n=264 [8.2%]) and chest pain (n=261 [8.1%]). The overall prevalence of any arrhythmia was 12.1%, with 44.1% of arrhythmias occurring after the first 48 hours of monitoring. Arrhythmias were detected in 10.0% of patients who were referred for palpitations, 6.7% of patients referred for syncope, 14.8% of patients referred for tachycardia, 22.7% of patients referred for paroxysmal SVT, and 6.5% of patients referred for chest pain.

In 2016, Solomon et al evaluated the diagnostic yield for potentially high-risk arrhythmias with 14 days of continuous recording with the Zio Patch among 122,454 patients (122,815 recordings) included in a manufacturer registry. Patients included in the series all underwent monitoring with the device from November 2011 to December 2013. Mean wear time was 9.6 days. Overall, there were 22,443 (18%) patients with sustained ventricular tachycardia, 1766 (1.4%) patients with sinus pauses of 3 seconds or more, 521 (0.4%) patients with AF pauses of 3 seconds or more, 249 (0.2%) patients with symptomatic pauses, and 1468 (0.4%) with high-grade heart block, which were considered potentially high-risk arrhythmias. After 24 and 48 hours of monitoring, 52.5% and 65.5%, respectively, of potentially high-risk arrhythmias were detected. Seven days of monitoring identified 92.9% of potentially high-risk arrhythmias.

Single-center studies, summarized in Table 2, have reported on the diagnostic yield and timing of detection of arrhythmias in patients monitored with the Zio Patch for a variety of arrhythmias. These studies generally have reported high rates of arrhythmia detection.

Health Quality Ontario (2017) published an assessment comparing long-term continuous AEMs with external cardiac loop recorders for detecting arrhythmias. The assessment included a systematic review of the literature on the effectiveness of both devices for detecting arrhythmias. No studies directly comparing long-term continuous AEMs with ELRs were found, so indirect comparisons were constructed using 24-hour Holter monitors as the common comparator. Twelve cohort studies were included; seven addressed long-term AEMs and five addressed ELRs. Using a meta-regression model to control for variation in device-wearing time and baseline syncope rate, the estimated difference between the long-term continuous AEMs and ELRs in their ability to detect arrhythmias was small (risk difference, 0.01; 95% confidence interval [CI], -0.18 to 0.20). Both devices were more effective than a 24-hour Holter. However, the quality of evidence was evaluated as poor using GRADE criteria.

Table 2: Single-Center Studies Reporting on Zio Patch Yield

Study	Patient Population	Monitoring Indication	Main Findings
Eisenberg et al (2014)	524 consecutive patients evaluated in an academic EP practice	• Surveillance for unspecified arrhythmia or palpitations: 47% • Known/suspected AF: 30% • Syncope: 8% • Bradycardia surveillance: 4% • Tachycardia surveillance: 5% • Chest pain 2%	• Significant arrhythmias detected in 297 (57%) • 66% had 1st arrhythmia detected within 2 d of monitoring • 25% of patient-triggered events associated with clinically significant arrhythmias
Schreiber et al (2014)	174 patients with symptoms suggestive of arrhythmia seen in an ED	• Palpitations: 44.8% • Syncope: 24.1% • Unspecified arrhythmias detected in the gIED: 11.5%	• >1 significant arrhythmia other than chronic AF (≥4 beats VT, paroxysmal AF, ≥4 beats SVT, ≥3-second pause, 2nd-degree Mobitz II or 3rd-degree AV block, or symptomatic bradycardia) detected in 83 (47.7%) • Median time to arrhythmia detection: o Any arrhythmia: 1.0 d (IQR, 0.2-2.8 d) o VT: 3.1 d o Sinus pause: 4.2 d o Significant heart block: 5.8 d

AF: atrial fibrillation; AV: atrioventricular; ED: emergency department; EP: electrophysiology; IQR: interquartile range; SVT: supraventricular tachycardia; VT: ventricular tachycardia.

Section Summary: Continuous Monitors with Longer Recording Periods

The available evidence on continuously worn cardiac monitors that can store data for longer periods of time than standard Holter monitoring indicates that such devices typically detect greater numbers of arrhythmias during extended follow-up than 24- or 48-hour Holter monitoring. There is not strong evidence to suggest that long-term continuous monitors are superior to external loop recorders in detecting arrhythmias.

Ambulatory Event Monitors in the Detection of AF

AF can be diagnosed on an electrocardiogram (ECG) or on Holter monitoring in individuals with suspected AF; however, a single ECG or short-term Holter monitor 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.

Patients with Atrial Fibrillation Treated with Catheter Ablation

Many patients with atrial fibrillation treated with catheter ablation are on long-term anticoagulation, and all patients treated with ablation are given anticoagulation for up to three

months post-procedure. In patients with an apparently successful ablation who do not show signs or symptoms of recurrent atrial fibrillation at time periods longer than three months post-ablation, the decision on whether to continue treatment with anticoagulants needs to be made. Studies have demonstrated that late recurrences are not uncommon following ablation and that these recurrent episodes are often asymptomatic. In addition, the presence of recurrent episodes of atrial fibrillation is a predictor of future thromboembolic events. In a larger observational study of 565 patients followed post-ablation, the two major predictors of thromboembolism were the CHADS score and the presence of recurrent episodes of atrial fibrillation.

Randomized Controlled Trials

In a prospective, randomized study, Kapa et al (2013) compared implantable loop monitors with conventional transtelephonic recorders in the assessment of arrhythmia burden after catheter ablation of AF. Forty-four patients were enrolled and randomized; all patients received the implantable loop recorder postablation. Six patients were excluded due to requests for device removal or loss to follow-up. During the first six months after ablation, all subjects underwent conventional monitoring that consisted of twice daily one-minute pulse rate assessments by the patient and three 30-day transtelephonic monitoring periods. At six months postablation, patients were allocated to the randomization arm (decided in a 1:1 manner at initial enrollment) of either the implantable loop recorder (transmission of data every 31 days) or conventional monitoring (twice daily one-minute pulse-rate assessment, and one trans-telephonic recording for 30 days at month 11). Over the first six months after ablation, conventional monitoring revealed AF in 7/38 patients (18%) and the implantable loop recorder confirmed AF in all of these patients. In an additional 11 patients (29%), AF was detected on implantable loop recorder. During the subsequent six- month period, 5/18 patients in the conventional monitoring arm refused ongoing monitoring due to discomfort and lifestyle restrictions; of the remaining 13, five had a recurrence of AF (38%). In the implantable loop recorder group, five of 20 patients had recurrence of AF. In the implantable loop recorder arm, 71% of the patients had their antiarrhythmic drugs discontinued compared with 44% in the conventional monitoring group over the randomization period (p=0.04).

Observational Studies

Reporting on the prospective DISCERN-AF (Discerning Symptomatic and Asymptomatic Episodes Pre and Post-Radiofrequency Ablation of AF) study, Verma et al (2013) evaluated the incidence of asymptomatic AF episodes following AF ablation (using an implantable cardiac monitoring) followed 50 patients with cardiac monitoring over 18 months postablation. Based on symptoms alone, 29 (58%) of 50 patients were arrhythmia-free after ablation; based on occurrence of symptoms or the detection of AF on intermittent (every 3 month) ECG or Holter monitor, 28 (56%) patients were arrhythmia-free postablation. Six (12%) patients had arrhythmias detected on implantable monitoring alone.

Several other observational studies have followed patients who stopped anticoagulation after an evaluation that includes ambulatory monitoring was negative for recurrent episodes. These patients appear to have a low subsequent rate of thromboembolic events. In one such study of 3,355 patients from five clinical centers, 2,692 discontinued anticoagulation at three to six months following ablation. During a mean follow-up of 28 months, two patients (0.07%) who were off anticoagulation experienced an ischemic stroke. This rate was not significantly different

from the rate of stroke in patients who continued anticoagulation (0.45%). The rate of major hemorrhage was lower for patients who were off anticoagulation compared to those who continued (2 vs. 0.04%, respectively; p<0.001).

Section Summary: Ambulatory Event Monitoring for AF after 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 of 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. These changes in management based on ambulatory monitoring are likely to lead to improved outcomes.

AEMs and Patients with Cryptogenic Stroke
Approximately 5% of patients with cryptogenic stroke will have atrial fibrillation diagnosed on ECG and/or telemetry monitoring in the hospital. The use of continuous telemetry monitoring has been compared to Holter monitoring for patients hospitalized for stroke or transient ischemic attack (TIA); these results are inconclusive as to which is the preferred method. Longer-term ambulatory event monitoring will identify additional patients with asymptomatic episodes, with rates of detection reported in the literature for an estimated 6-26% of patients.

Systematic Reviews
In 2015, Sposato et al reported results of a systematic review and meta-analysis of studies reporting rates of new AF diagnosis after cryptogenic stroke or TIA based on cardiac monitoring, stratified into four sequential phases of screening: Phase 1 (emergency room) 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; and Phase 4 (second ambulatory period) consisted of mobile cardiac outpatient telemetry, external loop recording, and implantable loop recording. 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, four (5%) stratified events into cryptogenic and non-cryptogenic, and 53 (67%) included unselected patient populations. The proportion of patients diagnosed with post-stroke AF was 7·7% (95% CI, 5.0 to 10.8) in Phase 1, 5.1% (95% CI, 3.8% to 6.5%) in Phase 2, 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 poststroke AF by MCOT (15.3%; 95% CI, 5.3% to 29.3%), external loop recording (16.2%; 95% CI, 0.3% to 24.6%), and implantable loop recording (16.9%; 95% CI, 10.3% to 24.9%; p=0.97).

Kishore et al conducted a systematic review and meta-analysis of prospective observational studies and RCTs that reported rates of detection of newly-diagnosed AF in patients with ischemic stroke or TIA who underwent any cardiac monitoring for at least 12 hours. Thirty-two studies were included: 18 studies that included patients with ischemic stroke only, one study that included TIA only, and 13 studies included both ischemic stroke and TIA. The authors 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% confidence interval [CI], 4.4% to 8.3%) and among selected patients was 13.4% (95% CI, 9.0% to 18.4%). In cryptogenic strokes, new AF was detected in 15.9% (95% CI, 10.9% to 21.6%). Among selected patients, the detection rate of AF 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 recorder, and MCOT) was 14.7% (95% CI, 10.7% to 19.3%).

The Kishore and other studies suggest that longer periods of cardiac monitoring increase the likelihood of AF detection. However, many of these asymptomatic episodes of AF are brief and the relationship to the preceding stroke uncertain, as there are other potential causes of asymptomatic stroke. 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.

Randomized Controlled Trials

There were four RCTs identified that evaluated ambulatory monitoring in patients with cryptogenic stroke. Two of these were small pilot trials. One small RCT published in 2013 randomized 40 patients with cryptogenic ischemic stroke or high-risk TIA to usual care or 21 days of MCOT (See Table 3). There were no cases of AF detected in either group (See Table 4). Two patients in the MCOT group had non-sustained ventricular tachycardia detected, which was of uncertain clinical significance in relation to their stroke.

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 (see Table 3). 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 followup. The difference did not differ statistically at 90-day follow-up (see Table 4).

In 2014, two larger RCTs were published. Sanna et al reported results from the CRYSTAL-AF study, an RCT to evaluate whether long-term monitoring of patients with cryptogenic stroke with implantable cardiac monitors (ICM) leads to changes in anticoagulant management and/or improved outcomes. The study 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 seen on computed tomography (CT) scan or magnetic resonance imaging (MRI), and no mechanism determined after a work-up that included 12-lead ECG, 24-hour Holter monitoring, transesophageal echocardiography, CT or magnetic resonance angiography of the head and neck, and hypercoagulability screening (for patients <55 years old). Analysis was intention-to-treat. Of the 441 randomly assigned patients, 416 (94.3%) completed six months of follow-up, two were lost to follow-up, five died, and 18 exited the study before six months. Crossover occurred in 12 patients in the ICM group and six 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). The median time from randomization to detection of AF was 41 days (interquartile range [IQR], 14-84) in the ICM group and 32 days (IQR, 2-73) in the control group. Most AF episodes in the ICM group were asymptomatic (74%), compared with 33% of those in the control group. The rate of AF detection was similarly greater in the ICM group at the 12-month follow-up point (12.4% vs 2.0%; HR=7.3; 95% CI, 2.6 to 20.8; p<0.001). The rate of use of oral anticoagulants was 10.1% in the ICM group versus 4.6% in the control group at six months (p=0.04) and 14.7% versus 6.0% at 12 months (p=0.007). Five of the 208 ICMs (2.4%) that were inserted were removed due to infection or erosion of the device pocket.

Also in 2014, Gladstone et al reported results from the EMBRACE study, an RCT that compared 30-day autotriggered cardiac event monitors with conventional 24-hour monitors for the detection of AF in patients with cryptogenic stroke (Table 3). Included patients were aged 55 or older, with no known history of AF, and an ischemic stroke or TIA of undetermined cause within the prior six months. All patients underwent standard screening for AF with one or more ECGs and one or more 24-hour Holter monitors. Five hundred seventy-two patients were randomized to receive an external event recorder (ER910AF Cardiac Event Monitor, Braemar) or 24-hour Holter monitoring. Among the intervention group subjects, 82% completed at least three weeks of monitoring. AF was detected in 45 of 280 patients (16.1%) in the intervention group, compared with 9 of 277 (3.2%) in the control group (risk difference, 12.9 percentage points; 95% CI, 8.0 to 17.6; p<0.001). At 90 days of follow-up, patients in the intervention group were more likely to be treated with anticoagulants than the control group (18.6% vs 11.1%; absolute treatment difference, 7.5 percentage points; 95% CI, 1.6 to 13.3; p=0.01).

Brachmann et al reported on 3-year follow-up from the CRYSTAL-AF trial in 2016. At the closure of the trial, 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<0.001).

Table 3. Summary of RCT Characteristics for AEM for Cryptogenic Stroke

					Interventions (n)	
Study	**Country**	**Sites**	**Dates**	**Participants**	**Active**	**Comparator**
Kamel et al (2013)	U.S.	1	2009-2011	Cryptogenic ischemic stroke or high-risk TIA	MCOT (20)	Standard (20)
Higgins et al (2013)	U.K.	2	2010-2011	Transient or persistent symptoms of acute TIA	ELR (50)	Standard (50)
Sanna et al (2014) & Brachmann et al (2016)	Canada, Europe, U.S	55	2009-2012	Cryptogenic ischemic stroke or TIA	ILR (221)	Standard (220)
Gladstone et al (2014)	Canada	16	NR	Cryptogenic ischemic stroke or TIA	ELR (280)	Standard (277)

AEMs: ambulatory event monitors; ELR: external loop recorder; ILR: implantable loop recorder; MCOT: mobile cardiac outpatient telemetry; NR: not reported RCT: randomized controlled trial; TIA: transient ischemic attack.

Table 4. Summary of RCT Results for AEMs for Cryptogenic Stroke

Study	FU	AF Detection			Additional Findings
		AEM%	Standard %	p	
Kamel et al (2013)	90 d	0	0	NS	• MCOT identified atrial tachycardia in 2 patients (1 incorrectly labeled as AF by telemetry software) • MCOT identified 2 nonsustained ventricular tachycardia
Higgins et al (2013)	14 d 90 d	18 22	2 8	<0.05 0.09	No difference between groups for recurrent stroke, TIA, or mortality
Sanna et al (2014); Brachmann et al (2016)	6 mo 12 mo 3 y	8.9 12.4 30	1.4 2.0 3.0	<0.001 <0.001 <0.001	• Percent patients on oral anticoagulation therapy significantly higher in ILR group vs standard group • At 3-y follow-up, recurrent stroke or TIA occurred in 20 patients in ILR group and in 24 in standard group
Gladstone et al (2014)	90 d	16.1	3.2	<0.001	Atrial premature beats was identified in a regression model as a potential predictor of AF detection

AEM: ambulatory event monitor; AF: atrial fibrillation; FU: follow-up; ILR: implantable loop recorder; MCOT: mobile cardiac outpatient telemetry; RCT: randomized controlled trial; TIA: transient ischemic attack.

Nonrandomized Studies

Nonrandomized and non-comparative studies published before the RCTs described above have reported on AF detection rates after cryptogenic stroke after long-term monitoring with various types of monitors, including implantable loop recorders, and continuous monitors with longer recording periods, along with a pilot study evaluating the Zio Patch for AF detection post-stroke.

Section Summary: AEMs and Patients with Cryptogenic Stroke

Randomized studies, including 2 large RCTs, have demonstrated that implantable and external loop recorders are associated with higher rates of detection of AF 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.

AEMs and AF Detection in Unselected Patients

Screening for AF in asymptomatic patients has been proposed to reduce burden of stroke. Evaluating the net benefits of screening for AF in unselected patients requires considering the potential risk of stroke in absence of screening, incremental benefit of earlier versus later treatment for stroke resulting from earlier detection of AF and potential harms of overdiagnosis.

Assessing the prevalence of asymptomatic AF is difficult because of the lack of symptoms. Approximately a third of patients with AF are estimated to be asymptomatic. Studies have suggested that most paroxysmalepisodes of AF are asymptomatic. It is uncertain whether

patients with paroxysmal AF have similar stroke risk compared to those with persistent or permanent AF; some studies have suggested the risk of stroke is similar while a 2016 meta-analysis of 12 studies (total N=99,996 patients) suggested risk for thromboembolism and all-cause mortality were higher with non-paroxysmal compared to paroxysmal AF. The clinical management of symptomatic and asymptomatic AF is the same. Anticoagulation should be initiated if reduction in risk of embolization exceeds complications due to increase bleeding risk.

Screening for AF in unselected patients could be either systematic or targeted to high risk populations. European guidelines for screening for AF are based on a large-cluster randomized controlled trial of opportunistic pulse taking versus systematic screening with 12-lead ECG or standard care in general practice which showed that systematic and opportunistic screening detected similar rates of AF and both were superior to standard care. The mechanisms of how and when to screen for AF in unselected populations, have not been well studied.

Randomized Controlled Trials

Halcox et al (2017) conducted an RCT (REHEARSE-AF), which screened patients for AF using the AliveCor Kardia monitor (n=500) or routine care (n=501). Patients were 65 years and older, asymptomatic, with CHADS-VASc scores of 2 or higher. Patients randomized to the Kardia monitor arm undertook twice-weekly 30-second single-lead iECG recordings and uploaded the information to a secure server. Analysis was performed using an automated software system and forwarded to a physiologist reading service. Abnormal ECG readings were sent to cardiologists. Appropriate care was arranged when arrhythmias were detected. Patients in the routine care arm were followed by their general practitioners. All patients were contacted at 12, 32, and 52 weeks. At 52-week follow-up, 19 patients in the Kardia monitor arm and 5 patients in the routine care arm were diagnosed with AF (HR=3.9; 95% CI, 1.4 to 10.4; p=0.007). There were no significant differences in the rates of mortality; stroke, TIA, or spontaneous embolism; deep vein thromboembolism or pulmonary embolism; or other cardiovascular events between groups.

Observational Studies

In 2015, Turakhia et al reported results of a single-center non-comparative study evaluating the feasibility and diagnostic yield of a continuously recording device with longer recording period (Zio® Patch) for AF screening in patients with risk factors for AF. The study included 75 patients over age 55 with at least two risk factors for AF (coronary disease, heart failure, hypertension, diabetes, or sleep apnea), without a history of prior AF, stroke, TIA, implantable pacemaker or defibrillator, or palpitations or syncope in the prior year. Of the 75 subjects, 32% had a history of significant valvular disease, and 9.3% had prior valve replacement. Most subjects were considered to be at moderate to high risk of stroke (CHA2DS2-VASc ≥2 in 97% of subjects). After a mean follow-up of 7.6 days, atrial fibrillation was detected in four subjects (5.3%), all of whom had CHA2DS2-VASc scores of greater than or equal to two. All patients with AF detected had an initial episode within the first 48 hours of monitoring. Five patients had episodes of atrial tachyarrhythmias lasting at least 60 seconds detected.

Narasimha et al (2018) published results of a study in which 33 patients wore both an ELR and a Kardia monitor to screen for AF during a period of 14 to 30 days. Patients were 18 years or older, had palpitations less often than daily but more frequently than several times per month, and prior nondiagnostic ECGs. Study personnel viewed the Kardia monitor recordings once

daily. A physician was contacted if a serious or sustained arrhythmia was detected. Patients were also monitored by the external loop recording company, which notified a physician on call when necessary. All 33 patients had a potential diagnosis using the Kardia monitor and 24 patients received a diagnosis using the ELR (p=0.001).

Section Summary: AF Detection in Unselected Patients

For the use of ambulatory monitoring for the diagnosis of AF in asymptomatic but higher risk patients, a small non-comparative study demonstrated that monitoring with the Zio Patch for a mean of 8 days resulted in a small percentage (5%) of AF detection. Two studies testing the Kardia monitor (1 RCT, 1 nonrandomized comparative study) reported that the Kardia monitor detected more arrhythmias than routine care and an ELR, respectively. However, none of these studies evaluating asymptomatic patients determined whether these measurements changed patient management. The RCT, which followed patients for one year, did not detect a difference in health outcomes between patients monitored using Kardia or routine care. The use of population-based screening for asymptomatic patients is not well-established, and several studies are underway to evaluate population-based screening and may influence the standard of care for AF detection in patients without symptoms or a history of stroke or TIA. To determine whether outcomes are improved for ambulatory monitoring for AF in patients without a history of stroke/TIA or treated AF, studies comparing the outcomes for various outpatient diagnostic screening strategies for AF would be needed.

Implantable Loop Recorders

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 that an ILR as an initial strategy may be reasonable.

Implantable Loop Recorders in Individuals with Signs/Symptoms of Arrhythmia

Systematic Reviews

Solbiati et al (2017) conducted a systematic review and meta-analysis on the diagnostic yield of ILRs in patients with unexplained syncope. 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 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.

In 2016, Burkowitz et al reported on a systematic review and meta-analysis of ILRs in the diagnosis of syncope and the detection of AF. These indications are discussed separately in this review. For the indication of syncope diagnosis, the review identified 3 RCTs comparing ILRs with a conventional diagnosis strategy, which was Holter monitoring in all 3 studies. In pooled

analysis, an ILR diagnosis strategy was associated with a higher likelihood of the end point of diagnostic yield (relative risk, 4.17; 95% CI, 2.57 to 6.77; I^2=14%).

Randomized Controlled Trials

A 2001 RCT reported by Krahn et al, compared a conventional monitoring strategy (external loop recorder monitoring for 2-4 weeks, followed by tilt-table and electrophysiologic testing) with at least 1 year of monitoring to an ILR in 60 subjects with unexplained syncope (n=30 per group) (See Table 5). Eligible patients had previously undergone 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 versus 52% of those in the ILR arm (p=0.012).

In 2004, Farwell et al reported results of an RCT comparing the diagnostic yield of an ILR (Reveal Plus, Medtronic) with a conventional diagnostic strategy in 201 patients with unexplained syncope (See Table 5). 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 (33%) had an ECG diagnosis than control patients (4%; HR for ECG diagnosis; 8.93; 95% CI, 3.17 to 25.19; p <0.001).Seven of the loop recorder patients had a diagnosis made with the device's autotrigger feature. In the loop recorder group, 34 patients had an ECG-directed therapy initiated (vs 4 in the control group; HR=7.9; 95% CI, 2.8 to 22.3). No device-related adverse events were reported.

Giada et al (2007) conducted an RCT of 2 diagnostic strategies in 50 patients with infrequent (≤1 episode per month) unexplained palpitations: an ILR strategy (n=26) vs a conventional strategy (n=24) including 24-hour Holter, 4 weeks of ambulatory ECG monitoring with an external recorder, and an electrophysiologic study if the 2 prior evaluations were negative) (See Table 5). 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 (±25) 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 (73%; vs conventional group, p<0.001) after a mean time to diagnosis of 279 (±228) days (See Table 6).

One small RCT by Da Costa et al (2013) compared the use of an implantable loop recorder with conventional follow-up in 78 patients with a first episode of syncope (See Table 5). A significant number of patients had cardiomyopathy (23%), atrial fibrillation (15.4%), and/or bundle branch block on ECG (58%). Mean follow-up time was 27 months. A total of 21 patients (27%) had at least one arrhythmia detected, with a significant difference in detection rate for the implantable loop recorder group (36.6%) compared to the conventional follow-up group (See Table 6).

In 2014, Podoleanu et al reported results of an open-label RCT comparing two strategies for evaluating syncope, an experimental strategy involving the early use of an implantable loop

recorder and a conventional strategy excluding an ILR (See Table 5). The study included patients who had a single syncope (if severe and recent), or at least two syncopes in the past 12 months. The syncope had to be unexplained at the end of clinical examination and a workup including 12-lead ECG, echocardiography, and head-up tilt-test. Patients randomized to implantable loop recorder received the Reveal or Reveal Plus device. After 14 months of follow up, a definitive cause of syncope was established in 18 (46.2%) of patients in the implantable loop recorder group and in two (5%) of conventionally-managed patients (p<0.001) (See Table 6). Arrhythmic causes of syncope in the implantable loop recorder group included two cases of atrioventricular (AV) block (5%), four cases of sinus node disease (10%), one case of AF (2.5%), one case of ventricular fibrillation (2.5%), and three other tachycardias (8%). In the conventionally-managed group, eight patients had a diagnosis of presumed reflex syncope.

Table 5. Summary of RCT Characteristics for ILRs for Arrhythmia

					Interventions (n)	
Study	**Country**	**Sites**	**Dates**	**Participants**	**Active**	**Comparator**
Podoleanu et al (2014)	France	13	2004-2008	Single recent syncope or 2 in past 12 mo	ILR (39)	Standard (39)
Da Costa et al (2013)	France	Multiple, NS	2005-2010	Single syncope	ILR (419)	Standard (37)
Giada et al (2007)	Italy	Multiple, NS	NR	Unexplained palpitations I	ILR (26)	Standard (24)
Farwell et al (2004)	England	1	2000-2001	≥2 unexplained syncope in past 12 mo	ILR (103)	Standard (98)
Krahn et al (2001)	England	1	NR	Single or recurrent unexplained syncope	ILR (27)	ELR (30)

ELR: external loop recorder; ILR: implantable loop recorder; NR: not reported; NS: not specified; RCT: randomized controlled trial.

Table 6. Summary of RCT Results for ILRs for Arrhythmia

Study	**FU**	**Diagnosis Made**			**Additional Findings**
		ILR (%)	**Standard (%)**	**p**	
Podoleanu et al (2014)	14 mo	18 (46)	2 (5)	<0.001	• Advanced cardiology tests performed less frequently in ILR group vs standard (p=0.05) • No difference in QOL
Da Costa et al (2013)	27 mo[a]	15 (37)	4 (11)	0.02	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)	≥12 mo	19 (73)	5 (21)	<0.001	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)	≥6 mo	34 (33)	4 (4)	<0.0001	• ECG-directed therapy was initiated quicker in the ILR group • No difference in syncopal episodes,

					mortality, or QOL
Krahn et al (2001)	12 mo	14 (52)	6 (20)	0.012	• 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=0.07)

ECG: electrocardiogram; FU: follow-up; HR: hazard ratio; ILR: implantable loop recorder; QOL: quality of life; RCT: randomized controlled trial. a Mean.

Observational Studies

In a report from an observational registry of patients who received or were about to receive an implantable loop recorder (the Reveal Plus, DX, or XT device) because of unexplained syncope, Edvarsson et al (2014) described the yield of monitoring in 570 patients who were implanted and followed for at least a year or until diagnosis. Most patients (97.5%) had a standard ECG prior to initiation of the implantable loop recorder, 11.8% had prior external loop recorder, and 54.6% had in-hospital ECG monitoring. During the monitoring period, 218 patients (38%) had recurrent syncope. The proportion of specific diagnoses based on the implantable loop monitor is not reported, but of the subjects who had a recurrence, 42.2% had a pacemaker implanted, 4.6% had an implantable cardioverter defibrillator implanted, 4.1% received antiarrhythmic drug therapy, and 3.7% underwent catheter ablation.

Other observational studies have reported on the diagnostic yield of arrhythmia in patients with symptoms monitored with ILRs. Bhangu et al (2016) reported on the diagnostic yield of ILRs in a series of 70 elderly patients with unexplained falls.

Implantable Loop Recorders in the Detection of Atrial Fibrillation

As noted in the preceding section on the detection of AF, some trials that have demonstrated improved outcomes with monitoring strategies (i.e., the CRYSTAL AF) used ILRs. Implantable autotrigger loop recorders have also been developed that are specifically geared toward detection of atrial fibrillation through the use of atrial fibrillation detection algorithms. Several nonrandomized studies have evaluated the accuracy of implantable autotriggered loop recorders for the diagnosis of AF.

Systematic Reviews

In 2015, Afzal et al reported on a systematic review and meta-analysis of studies comparing ILRs with wearable AEMs for prolonged outpatient rhythm monitoring after cryptogenic stroke. The review 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, 50-569 days), while for wearable device-monitored patients, the median monitoring duration was 14 days (range, 4-30 days). Compared with wearable device AEMs, ILRs were associated with significantly higher rates of AF detection (23.3% vs 13.6%; odds ratio, 4.54; 95% CI, 2.92 to 7.06; $p<0.05$).

In the 2016 Burkowitz review (described above), for the indication of cryptogenic stroke, 1 RCT and 5 non-comparative studies met inclusion criteria. The sole RCT identified by Sanna et al is described above.

Observational Studies

Hanke et al (2009) compared an implantable autotrigger device with 24-hour Holter monitoring done at three-month intervals in 45 patients who had undergone surgical ablation for atrial fibrillation. After a mean follow-up of 8.3 months, the implantable loop recorder identified atrial fibrillation in 19 patients (42%) in whom Holter monitoring recorded sinus rhythm.

Hindricks et al (2010) evaluated the accuracy of an implantable autotriggered loop recorder in 247 patients at high risk for paroxysmal atrial fibrillation. All patients underwent simultaneous 46-hour continuous Holter monitoring, and the authors calculated the performance characteristics of the loop recorder using physician-interpreted Holter monitoring as the criterion standard. The sensitivity of the loop recorder for detecting atrial fibrillation episodes of two minutes or more in length was 88.2%, rising to 92.1% for episodes of six minutes or more. Atrial fibrillation was falsely identified by the loop recorder in 19 of 130 patients who did not have atrial fibrillation on Holter monitoring, for a false-positive rate of 15%. The atrial fibrillation burden was accurately measured by the loop recorder, with the mean absolute difference between the loop recorder and Holter monitor of 1.4%.

In 2015, Ziegler et al reported on a large (N=1247) set of patients undergoing ILR monitoring for AF detection after a cryptogenic stroke who were identified from the manufacturer's registry. Over a median follow-up of 182 days, a total of 1521 episodes of AF were detected in 147 patients. Overall, 42 (29%) patients had a single episode of AF and 105 (71%) patients had multiple episodes. The overall detection rate 12.2% (at 182 days) was somewhat higher than that reported in CRYSTAL AF.

Nolker et al (2016) published results of the DETECT AF study, in which readings from an implantable cardiac monitor (Confirm ICM, St. Jude Medical) were compared with readings from a Holter monitor used for 4 days at least 2 weeks post implant. Patients had either been diagnosed with or had a clinical suspicion of paroxysmal AF (n=90). Due to difficulties with synchronizing the Holter monitor and the implanted device, data from only 79 patients were used in calculations. Patient-level sensitivity, positive predictive value, specificity, and negative predictive value were 100%, 64%, 86%, and 84%, respectively. Episode-level sensitivity, positive predictive value, specificity, and negative predictive value were 95%, 64%, 87%, and 76%, respectively.

Sanders et al (2016) reported on the diagnostic yield for AF with the Reveal Linq device, a miniaturized ILR with a detection algorithm designed to detect AF in a nonrandomized, prospective trial. The study included 151 patients, most of whom (81.5%) were undergoing monitoring for AF ablation or AF management. Compared with Holter-detected AF, the ILR had a diagnostic sensitivity and specificity for AF of 97.4% and 97.0%.

Ciconte et al (2017) published results from 66 patients with documented AF or symptoms attributable to AF, who were given an implantable monitoring device (BioMonitor). Recordings from the monitoring device were compared with 48-hour Holter monitoring results performed 4 weeks after implantation. Sensitivity and positive predictive value for AF detection of the implantable monitoring device were 95% and 76%, respectively.

Safety of Implantable Loop Recorders

In 2015, Mittal et al reported on safety outcomes related to the use of an ILR, the Reveal LINQ device, based on data from 2 studies, the Reveal LINQ Usability study and the Reveal LINQ Registry. 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 postmarketing 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 version used in these studies measures $7 \times 45 \times 4$ mm^3, and 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 were 1.6% and 1.6%, respectively, in the Registry study.

Section Summary: Implantable Loop Recorders

Studies of prolonged use of ILRs in patients have reported high rates of arrhythmia detection 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 Holter monitor.

Mobile Cardiac Outpatient Telemetry

This section addresses whether the addition of real-time monitoring to ambulatory cardiac monitoring (MCOT) is associated with improved outcomes. Two factors must be addressed in evaluating MCOT: (1) the inherent detection capability of the monitoring devices and (2) whether the real-time transmission and interpretation of data confers an incremental health benefit. The proposed addition of real-time monitoring suggests that there may be a subset of individuals who require immediate intervention when an arrhythmia is detected. Because it is not clear which patients comprise that subset, or whether identification of those patients in the outpatient setting leads to improved outcomes, such as reduced risks of sudden cardiac death, the evaluation of the second factor requires studies that directly assess outcomes, not just arrhythmia detection rates.

Randomized Controlled Trials

One randomized controlled trial was identified that compared MCOT to standard event monitors. This 2007 study involved 305 patients who were randomly assigned to the LOOP recorder or MCOT and who were monitored for up to 30 days. The unblinded study enrolled patients at 17 centers for whom the investigators had a strong suspicion of an arrhythmic cause of symptoms including those with symptoms of syncope, presyncope, or severe palpitations occurring less frequently than once per 24 hours and a non-diagnostic 24-hour Holter or telemetry monitor within the prior 45 days. Test results were read in a blinded fashion by an electrophysiologist. The majority of patients in the control group had a patient-triggered event monitor. Only a subset of patients (n=50) had autotrigger devices, thus precluding a comparison between MCOT and auto-trigger devices. Of the 305 patients, 266 completed at least 25 days of monitoring.

A diagnostic endpoint (confirmation/exclusion of arrhythmic cause of symptoms) was found in 88% of MCOT patients and in 75% of LOOP patients (p=0.008). The difference in rates was primarily due to detection of asymptomatic (not associated with simultaneous symptoms) arrhythmias in the MCOT group consisting of rapid atrial fibrillation and/or flutter (15 patients vs. one patient) and ventricular tachycardia defined as more than three beats and rate greater than 100 (14 patients vs. two patients). These differences were thought to be clinically significant rhythm disturbances and the likely causes of the patients' symptoms. The authors 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. In this study, the median time to diagnosis in the total study population was seven days in the MCOT group and nine days in the LOOP group.

Observational Studies

A number of uncontrolled case series report on arrhythmia detection of MCOT. One such published study by Joshi et al (2005) described the outcomes of a consecutive case series of 100 patients. Patients with a variety of symptoms were included, including, most commonly, palpitations (47%), dizziness (24%), or syncope (19%), as well as efficacy of drug treatment (25%). Clinically significant arrhythmias were detected in 51% of patients, but half of these patients were asymptomatic. The authors comment that the automatic detection results in an increased diagnostic yield, but there was no discussion of its unique feature, i.e., the real-time analysis, transmission, and notification of arrhythmia.

Kadish et al (2010) evaluated the frequency with which events transmitted by MCOT represented emergent arrhythmias, thereby indirectly assessing the clinical utility of real-time outpatient monitoring. A total of 26,438 patients who had undergone MCOT during a 9-month period were retrospectively examined. Of these patients, 21% (5459) had an arrhythmic event requiring physician notification, and 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 6 seconds or longer, and 42 with sustained bradycardia at less than 30 beats per minute.

Derkac et al (2017) retrospectively reviewed the BioTelemetry database of patients receiving ambulatory ECG monitoring, selecting patients prescribed MCOT (n=69,977) and patients prescribed AT-LER, an autotrigger looping event recorder (n=8513). Patients were diagnosed with palpitations, syncope and collapse, AF, tachycardia, and/or TIA. Patients given the MCOT 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 MCOT 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 SVT, and 222% higher for ventricular tachycardia. Mean time to diagnosis for each asymptomatic arrhythmia was shorter for patients monitored by MCOT than by AT-LER. There was no discussion of management changes or health outcomes based on monitoring results.

AF Detection

In an uncontrolled case series, Tayal et al (2008) reported on a retrospective analysis of patients with cryptogenic stroke, who had not been diagnosed with atrial fibrillation by standard

monitoring. In this study, 13 of 56 patients (23%) with cryptogenic stroke were found to have atrial fibrillation with MCOT. Twenty-seven asymptomatic atrial fibrillation episodes were detected in the 13 patients, 23 of these were shorter than 30 seconds in duration. In contrast, in 2015 Kalani et al reported a diagnostic yield for AF of 4.7% (95% CI, 1.5% to 11.9%) in a series of 85 patients with cryptogenic stroke. In this series, 82.4% of patients had completed transesophageal echocardiography, cardiac magnetic resonance imaging (cMRI), or both, with negative results. Three devices were used and described as MCOT devices: 34% LifeStar ACT ambulatory cardiac telemetry, 41% LifeStar AF Express auto-detect looping monitor, and 25% Cardiomedix cardiac event monitor. While the authors reported that there was a system in place to send the data for review, it is not clear if data were transmitted "real-time."

In a 2013 retrospective cohort study, Miller et al retrospectively analyzed paroxysmal AF detection rates among 156 patients who were evaluated with MCOT within six months of a cryptogenic stroke or TIA. Over a median period of MCOT monitoring of 21 days (range: one to 30 days), AF was detected in 17.3% of patients. The mean time to first occurrence of AF was 8.8 days (range: one to 21 days).

In the largest study evaluating the diagnostic yield of MCOT for AF, Favilla et al (2015) reported results of a retrospective cohort study of 227 patients with cryptogenic stroke or TIA who underwent 28 days of monitoring with mobile cardiac outpatient telemetry. AF was detected in 14% of patients (31/227), of whom three reported symptoms at the time of AF. Oral anticoagulation was initiated in 26 patients (84%) diagnosed with AF. Of the remaining five (16%) who were not anticoagulated, one had a prior history of gastrointestinal bleeding, three were not willing to accept the risk of bleeding, and one failed to follow up.

Section Summary: Mobile Cardiac Outpatient Telemetry

The available evidence suggests that MCOT is likely at least as good at detecting arrhythmias as ambulatory event monitoring. Compared with ambulatory event monitoring, MCOT is associated with the theoretical advantage of real-time monitoring, allowing for emergent intervention for potentially life-threatening arrhythmias. One study reported that 1% of arrhythmic events detected on MCOT over a 9- month period could be considered potentially emergent. However, no studies were identified that addressed whether the use of MCOT 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. There is insufficient evidence to demonstrate a clinically significant incremental benefit of MCOT.

Summary of Evidence

Ambulatory Event Monitoring

For individuals with signs and/or symptoms suggestive of arrhythmia(s) who receive patient- or auto-activated external ambulatory event monitoring or continuous ambulatory monitoring storing information for more than 48 hours, the evidence includes prospective and retrospective studies reporting on the diagnostic yield. Relevant outcomes are overall survival and morbid events. Studies have shown that continuous monitoring with longer recording periods clearly detect more arrhythmias than 24- or 48-hour Holter monitoring. Particularly for patients in who would, without the more prolonged monitoring, only undergo shorter term monitoring, the

diagnostic yield is likely to identify arrhythmias that may have therapeutic implications. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with atrial fibrillation (AF) following ablation who receive long-term ambulatory cardiac monitoring, the evidence includes randomized controlled trials (RCTs) comparing ambulatory event monitoring to standard care and several observational studies. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. RCTs evaluating a long-term monitoring strategy after catheter ablation for AF report significantly higher rates of AF detection with longer term ambulatory monitoring. The available evidence suggests that long-term monitoring for AF after postablation is associated with improved outcomes. However, the specific type of monitoring associated with the best outcomes is not well-defined. Trials that have demonstrated improved outcomes have used event monitors or implantable monitors. 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 a meaningful improvement in the net health outcome.

For individuals who have cryptogenic stroke with a negative standard workup for AF who receive long-term ambulatory cardiac monitoring, the evidence includes systematic reviews of RCTs comparing ambulatory event monitoring 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 implantable monitors. In addition, there are individual patient considerations that may make one type of monitor preferable over another. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic with risk factors for AF who receive long-term ambulatory cardiac monitoring, the evidence includes an RCT and 2 non-randomized studies. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. The studies showed use of the ambulatory monitors would result in higher AF detection compared with routine care. However, the RCT followed patients for one year and did not detect a difference in stroke occurrence between the monitored group and the standard of care group. The other studies did not discuss changes in patient management or health outcomes based on monitoring. Studies reporting on improved outcomes with longer follow-up are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

Implantable Loop Recording (ILR)

For individuals with 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 (ILRs) 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 of prolonged ILRs in patients have reported high rates of arrhythmia detection compared with external event monitoring or Holter monitoring. These studies support 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 a meaningful improvement in the net health outcome.

Outpatient Cardiac Telemetry

For individuals with signs and/or symptoms suggestive of arrhythmia who receive outpatient cardiac telemetry, the evidence includes 1 RCT and nonrandomized studies evaluating rates of arrhythmia detection with outpatient cardiac telemetry. Relevant outcomes are overall survival and morbid events. The available evidence has suggested that outpatient cardiac telemetry is at least as good at detecting arrhythmias as ambulatory event monitoring. However, studies have not evaluated whether the real-time monitoring feature of outpatient cardiac telemetry leads to reduced cardiac events and mortality. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

International Society for Holter and Noninvasive Electrocardiology et al

In 2017, the International Society for Holter and Noninvasive Electrocardiology and the Heart Rhythm Society (HRS) issued a consensus statement on ambulatory electrocardiogram and external monitoring and telemetry. Below are two summary tables from the consensus statement, detailing advantages and limitations of ambulatory electrocardiogram techniques (see Table 7) and recommendations for the devices that are relevant to this evidence review (see Tables 8).

Table 7. Advantages and Limitations of Ambulatory ECG Techniques

ECG Monitoring Technique	Advantages	Limitations
Holter monitoring	• Records and documents continuous 3- to 32-lead ECG signal simultaneously with biologic signals during normal daily activities • Physicians familiar with analysis software and scanning services	• Frequent noncompliance with symptom logs and event markers • Frequent electrode detachments • Signal quality issues due to skin adherence, tangled wires, dermatitis • Absence of real-time data analysis • Poor patient acceptance of electrodes
Patch ECG monitors	• Long-term recording of >14 d • Excellent patient acceptance	• Limited ECG from closely spaced electrodes, lacking localization of arrhythmia origin • Inconsistent ECG quality due to body type variations
External loop recorders	• Records only selected ECG segments marked as events either automatically or manually by patient • Immediate alarm generation on event detection	• Single-lead ECG, lacking localization of arrhythmia origin • Cannot continuously document cardiac rhythm • Requires patient to wear electrodes continuously
Event recorders	• Records only selected ECG segments after an event is detected	• Single-lead ECG, lacking localization of arrhythmia origin

	by patient • Immediate alarm generation at event detected by patient • Well-tolerated by patient	• Cannot continuously document cardiac rhythm • Diagnostic yield dependent on patient ability to recognize correct symptom
Mobile cardiac telemetry	• Multilead, so higher sensitivity and specificity of arrhythmia 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	• Long-term patient acceptance is reduced due to requirement of daily electrode changes

ECG: electrocardiogram.

Table 8. Select Recommendations for Ambulatory ECG and External Monitoring or Telemetry

Recommendation	COR[a]	LOE[b]
Selection of ambulatory ECG		
Holter monitoring when symptomatic events anticipated within 48 h	I	B-NR
Extended ambulatory ECG (15-30 d) when symptomatic events are not daily or are uncertain	I	B-R
Continuous monitoring (1-14 d) to quantify arrhythmia burden and patterns	I	B-NR
Specific conditions for use of ambulatory ECG		
Unexplained syncope, when tachycardia suspected	I	B-R
Unexplained palpitation	I	B-R
Detection of AF, triggering arrhythmias, and post-conversion pauses	IIa	B-NR
Cryptogenic stroke, to detect undiagnosed AF	I	B-R

AF: atrial fibrillation; ECG: electrocardiogram; COR: class of recommendation; LOE: level of evidence. 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.

American College of Cardiology, American Heart Association et al

In 2014, the American College of Cardiology (ACC), the American Heart Association (AHA), and the Heart Rhythm Society issued guidelines on the management of patients with AF. These guidelines recommend 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 same associations collaborated on guidelines in 2017 on the evaluation and management of patients with syncope. Cardiac monitoring recommendations are summarized below in Tables 9 and 10.

Table 9. Cardiac Monitoring Recommendations for Patients with Syncope

Recommendation	COR[a]	LOE[b]
Choice of a specific cardiac monitor should be determined on the basis of frequency and nature of syncope events.	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, transtelephonic monitor, external loop recorder, patch recorder, and MCOT.	IIa	B-NR
To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, an implantable cardiac monitor can be useful	IIa	B-R

COR: class of recommendation; LOE: level of evidence; MCOT: mobile cardiac outpatient telemetry. 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; C-EO: consensus of expert opinion based on clinical experience.

Table 10. Patient Selection Recommendations by Cardiac Rhythm Monitor

Type of Monitor	Patient Selection
Holter monitor	Symptoms frequent enough to be detected within 24 to 72 h
Patient-activated event monitor	• Frequent spontaneous symptoms likely within 2 to 6 wk • Limited use when syncope associated with sudden incapacitation
External loop recorder (patient or autotriggered)	Frequent spontaneous symptoms likely to occur within 2 to 6 wk
External patch recorder	• Alternative to external loop recorder • Leadless, so more comfortable, resulting in improved compliance • Offers only 1-lead recording
Mobile cardiac outpatient telemetry	• Spontaneous symptoms related to syncope and rhythm correlation • High-risk patients needing real-time monitoring
Implantable cardiac monitor	Recurrent, infrequent, unexplained syncope

The American College of Cardiology and the American Heart Association (1999) published guidelines for the use of ambulatory electrocardiography.78 The guidelines recommended ambulatory electrocardiography for two indications, unexplained syncope and unexplained recurrent palpitations, but did not explicitly distinguish between continuous (i.e., Holter monitoring) and intermittent (i.e., ambulatory event monitoring) monitoring. Regarding the effectiveness of antiarrhythmic therapy, the guidelines listed one class I indication: "To assess antiarrhythmic drug response in individuals in whom baseline frequency of arrhythmia has been well characterized as reproducible and of sufficient frequency to permit analysis." The guidelines did not specify whether Holter monitoring or ambulatory event monitors are most likely to be used. However, accompanying text noted that intermittent monitoring may be used to confirm the presence of an arrhythmia during symptoms. There were no class I indications for detection of myocardial ischemia. In addition, there were no class I indications for ambulatory monitoring to assess risk for future cardiac events in patients without symptoms of arrhythmia.

Heart Rhythm Society, European Heart Rhythm Association, et al

A consensus document on catheter and surgical ablation for atrial fibrillation was published in 2012 by the Heart Rhythm Society, the European Heart Rhythm Association, and the European Cardiac Arrhythmia Society. This document did not contain formal clinical practice guidelines, but provided general recommendations based on literature review and expert consensus. The use of AEMs post-ablation was addressed in two sections of the document. First, in the section discussing the use of anticoagulation following ablation, the following statement was made:

- Patients in whom discontinuation of systemic anticoagulation is being considered should consider undergoing continuous ECG monitoring to screen for asymptomatic Atrial Fibrillation/Atrial Flutter/Atrial Tachycardia.

In the section of the document dealing with postoperative rhythm monitoring of patients who are post-ablation the following statements were made:

> "The success of AF ablation is based in large part on freedom from AF recurrence based on ECG monitoring. Arrhythmia monitoring can be performed with the use of noncontinuous or continuous ECG monitoring tools."

The statement referenced a table of ambulatory cardiac monitoring devices (Holter, patch, external loop, implantable loop, wearable multisensors, Smartphone monitors), describing unique features of each. The table did not evaluate the safety or efficacy of these devices, nor recommend one over another.

European Heart Rhythm Association

In 2009, EHRA published guidelines on the use of diagnostic implantable and external loop recorders. For the indications that EHRA considered established at the time of publication, the guidelines make the following statements about indications for implantable and external recorders:

Class I recommendations:

- "ILR [implantable loop recorder] is indicated:
    - "In an early phase of evaluation of patients with recurrent syncope of uncertain origin who have:
        - "absence of high-risk criteria that require immediate hospitalization or intensive evaluation…"; and
        - "a likely recurrence within battery longevity of the device (LOE A)."
- "ELRs [external loop recorders] are indicated in patients with recurrent palpitations, undocumented by conventional ECG techniques, who have: inter-symptom interval <4 weeks and absence of high-risk criteria…which require immediate hospitalization or intensive evaluation (LOE B)."

Class IIa recommendations:

- "ILR may be indicated to assess the contribution of bradycardia before embarking on cardiac pacing in patients with suspected or certain neurally mediated syncope presenting with frequent or traumatic syncopal episodes (Level of evidence B)."

- "ILRs may be indicated in selected cases with severe infrequent symptoms when ELRs and other ECG monitoring systems fail to document the underlying cause (Level of evidence B)."
- "ELRs [external loop recorder] may be indicated in patients with recurrent (pre)syncopes who have:
    - "inter-symptom interval of ≤4 weeks, and
    - "suspicion of arrhythmic origin and
    - "absence of high-risk criteria that require immediate hospitalization or intensive evaluation…(Level of evidence B)."

American Academy of Neurology

In 2014, the American Academy of Neurology released updated guidelines on the prevention of stroke in patients with nonvalvular atrial fibrillation (NVAF). These guidelines make the following recommendations regarding 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 of evidence: C).
- Clinicians might obtain cardiac rhythm studies for prolonged periods (e.g., for one 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 of evidence: C).

U.S. Preventive Services Task Force Recommendations

Not applicable.

Key Words:

Ambulatory device monitors, continuous "memory loop" devices, implantable continuous "memory loop" devices, Reveal ® XT ICM, autotriggered devices, ambulatory event monitors, autotrigger, loop recorder, ER920W, Zio™ Event Card, ER920W Wireless. HeartrackSmart™ Wireless, Genesis 30-day Event Monitor, Cardio R® device, REKA E100™ system, Reveal LINQ™, Explorer™ Looping Monitor, LifeStar AF Express™ Auto-Detecting Looping Monitor, LifeWatch, Mobile outpatient cardiac telemetry, MCOT, outpatient cardiac telemetry, OCT, Verite´, Zio® Patch, Zio™ ECG Utilization Service, ZEUS, VectraplexECG™, BodyGuardian Remote Monitoring System™, HeartLinkII™, VST™, LifeStar™ ACT, CardioNet®, SEEQ™

Approved by Governing Bodies:

Some of the newer devices are described in the Description section for informational purposes. However, because there may be many devices within each category, a comprehensive description of individual devices is beyond the scope of this review.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply.
FEP: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:

CPT Codes:

The implantation and removal of an insertable loop recorder are coded as follows:

33282	Implantation of patient-activated cardiac event recorder
33284	Removal of an implantable, patient-activated cardiac event recorder

The interpretation of the electrocardiograms recorded with AEMs may be coded as follows:

93268	External patient and, when performed, auto- activated electrocardiographic rhythm derived event recording with symptom related memory loop with remote download capability up to 30 days,, 24-hour attended monitoring; includes transmission review and interpretation by a physician or other qualified health care professional.

Other CPT codes that can be used for AEM monitoring represent unbundling of the 93268 code:

93270	; recording (includes connection, recording and disconnection)
93271	; monitoring, transmission download and analysis
93272	; review and interpretation by a physician or other qualified health care professional.

There are specific CPT codes for mobile outpatient cardiac telemetry:

93228	External mobile cardiovascular telemetry with electrocardiographic recording, concurrent computerized real time data analysis and greater than 24 hours of accessible ECG data storage (retrievable with query) with ECG triggered and patient selected events transmitted to a remote attended surveillance center for up to 30 days; review and interpretation with report by a physician or other qualified health care professional
93229	; technical support for connection and patient instructions for use, attended surveillance, analysis and transmission of daily and emergent data reports as prescribed by a physician or other qualified health care professional

There are category III CPT codes for devices with longer recording capabilities:

0295T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; includes recording, scanning analysis with report, review and interpretation **(Effective 01/01/2012)**
0296T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; recording (includes connection and initial recording) **(Effective 01/01/2012)**
0297T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; scanning analysis with report **(Effective 01/01/2012)**
0298T	External electrocardiographic recording for more than 48 hours up to 21 days by continuous rhythm recording and storage; review and interpretation **(Effective 01/01/2012)**

HCPCS Codes:

E0616	Implantable cardiac event recorder with memory, activator and programmer

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Policy History:

Medical Policy Group, June 2009 **(2)**
Medical Policy Administration Committee, June 2009
Available for comment June 5-July 20, 2009
Medical Policy Group, June 2010 **(2)**
Medical Policy Administration Committee, June 2010
Available for comment, June 18-August 2, 2010
Medical Policy Group, December 2010; 2011 Coding update
Medical Policy Group, December 2010
Medical Policy Group, March 2011 **(2)**
Medical Review Committee, March 2011
Medical Policy Administration Committee, March 2011
Medical Policy Group, May 2011 **(2)**
Medical Review Committee, June 2011
Medical Policy Administration Committee, June 2011
Available for comment June 8 – July 25, 2011
Medical Policy Panel, October 2011
Medical Policy Group, December 2011 **(2):** Description and References updated
Medical Policy Group, December 2011 **(3):** Added 2012 'T' codes effective January 1, 2012
Medical Policy Group, June 2012 **(2):** Policy statement updated to include coverage of auto activated external ambulatory event monitors for patients with atrial fibrillation to monitor for asymptomatic episodes to evaluated response to treatment. Updated Key Points, Key Words, References
Medical Policy Administration Committee, June 2012

Available for comment June 26 through August 9, 2012
Medical Policy Panel, November 2012
Medical Policy Group, November 2012 **(2):** Policy updated with literature search through October 2012. Medically necessary indication for use of event monitors in patients with atrial fibrillation treated with catheter ablation revised to be consistent with recent guidelines. Investigational indication for patients for monitoring with including but not limited to monitoring effectiveness of antiarrhythmic medications for patients with cryptogenic stroke, and detection of myocardial ischemia by detecting ST segment changes.
Medical Policy Group, December 2012 **(3)**: 2013 Coding update – Verbiage update to Codes **93268 and 93272 effective 01/01/2013**.
Medical Policy Group, December 2012 **(3):** 2013 Coding Update: Verbiage change to Codes **93228**& **93229**-added "by a physician or other qualified health care professional". Effective 01/01/2013.
Medical Policy Administration Committee, January 2013
Available for comment January 10 through February 23, 2013
Medical Policy Panel, October 2013
Medical Policy Group, December 2013 **(2):** Medical criteria for coverage for implantable loop monitors revised from "…a prior trial of Holter monitor and other external ambulatory event monitors has been unsuccessful" to "…a prior trial of other external ambulatory event monitors has been unsuccessful." Key Points and References updated with information from literature search through August 2013. Note—there is no new information in BCBSA policy 2.02.08 that will change the retired BCBSAL Holter Monitor or MCOT policies.
Medical Policy Administration Committee, January 2014
Available for comment January 9 through February 23, 2014
Medical Policy Group, March 2014 **(3):** Update to Description, Key Points, Key Words, Governing Bodies, & References with available equipment Verite´ by eCardio
Medical Policy Panel July 2014
Medical Policy Panel, November 2014
Medical Policy Group, January 2015 **(3):** 2014 Updates to Description, Key Points, Key Words, Governing Bodies & References; no change in policy statement; status remains unchanged
Medical Policy Group, January 2015 **(3)**: 2014 Updates to Description, Key Points, Key Words & References; Policy statement updated effective February 1, 2015, to add situation of "Patients with cryptogenic stroke who have a negative standard work-up for atrial fibrillation including a 24-hour Holter monitor" to the use of patient-activated or auto-activated external ambulatory event monitors that meet medical criteria for coverage; removed patients with cryptogenic stroke from list of investigational other uses; refer also to literature updates for retired medical policies #460 and #461 – no change in policy statement on those
Available for comment February 4 through March 20, 2015
Medical Policy Panel, April 2015
Medical Policy Group, May 2015 **(4):** Update to policy statement to indicate that the use of an implantable monitor is medically necessary for the evaluation of cryptogenic stroke.
Available for comment May 30 through July 12, 2015
Medical Policy Panel, July 2015
Medical Policy Group, July 2015 **(4):** Updates to Description, Key Points, Key Words, and References. Added "and are considered investigational" to policy statement for clarification purposes. No change in policy intent.

Medical Policy Group, July 2015 **(4)**: Updates to Key Points and References. No change to policy statement.
Medical Policy Panel, May 2016
Medical Policy Group, March 2017 **(4):** Incorporated MP# 460 – *Mobile Cardiac Outpatient Telemetry and Hybrid Devices* into this policy and MP# 460 was archived. Title updated to include MCOT and added information throughout policy pertaining to MCOT. Updates to Description, Key Points, Key Words, Approved Governing Bodies, Current Coding, References, and Policy History. Added CPT codes 0295T-0298T, 93228 and 93229 to Current Coding section. Updated policy section by adding coverage for continuous ambulatory monitors that record and store information for periods >48 hours, updated coverage indications for implantable AEMs to include AF after an ablation, transferred MCOT policy statement to this policy which remains investigational (no change in this statement). Removed all language related to "hybrid" throughout the policy.
Medical Policy Administration Committee, April 2017
Available for comment March 18 through May 1, 2017
Medical Policy Panel, May 2017
Medical Policy Group, May 2017 **(4):** Updates to Description, Key Points, and References. No change to policy statement.
Medical Policy Panel, May 2018
Medical Policy Group, May 2018 **(4):** Updates to Description, Policy, Key Points, and References. Added 2 IV points to the IV statement for mobile apps and monitoring asymptomatic patients with risk factors for arrhythmia. Update did not change policy intent. Removed policy statements effective for dates of service February 1, 2015 – May 31, 2015 and February 25, 2014 – January 31, 2015.
Medical Policy Administration Committee, June 2018