

Ambulatory Event Monitors and Mobile Cardiac Outpatient Telemetry

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I. Description

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

Ambulatory Event Monitoring

For individuals who have signs and/or symptoms suggestive of arrhythmia(s) who receive patient- or autoactivated 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 detects more arrhythmias than 24- or 48-hour Holter monitoring. Particularly for patients who, without the more prolonged monitoring, would 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 who have AF following ablation who receive long-term ambulatory cardiac monitoring, the evidence includes a randomized controlled trial (RCT) comparing ambulatory event monitoring with standard care and several observational studies. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. The RCT evaluating a long-term monitoring strategy after catheter ablation for AF reported significantly higher rates of AF detection. The available evidence has suggested that long-term monitoring for AF postablation is associated with improved outcomes. However, 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 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 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 are asymptomatic with risk factors for AF who receive long-term ambulatory cardiac monitoring, the evidence includes an RCT and 2 nonrandomized 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 1 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

For individuals who have signs and/or symptoms suggestive of arrhythmia with infrequent symptoms who receive patient- or autoactivated implantable ambulatory event monitoring, the evidence includes RCTs comparing implantable loop recorders with shorter term monitoring, usually 24- to 48-hour Holter monitoring. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. Studies assessing prolonged implantable loop recorders in patients have reported high rates of arrhythmia detection compared with shorter external event or Holter monitoring. These studies have supported use of a progression in diagnostics from an external event monitor to implantable loop recorder 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 who have signs and/or symptoms suggestive of arrhythmia who receive outpatient cardiac telemetry, the evidence includes an RCT and nonrandomized studies evaluating rates of arrhythmia detection using 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.

BACKGROUND

CARDIAC ARRHYTHMIAS

Cardiac monitoring is routinely used in the inpatient setting to detect acute changes in heart rate or rhythm that may need urgent response. For some conditions, a more prolonged period of monitoring in the ambulatory setting is needed to detect heart rate or rhythm abnormalities that may occur infrequently. These cases may include the diagnosis of arrhythmias in patients with signs and symptoms suggestive of arrhythmias as well as the evaluation of paroxysmal 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 in some cases may be described as dizziness. An electrocardiogram (ECG) is generally indicated whenever there is suspicion of a cardiac cause of syncope. Some arrhythmic causes will be apparent on ECG. However, for patients in whom an ECG is not diagnostic, longer monitoring may be indicated. The 2009 joint guidelines from the European Society of Cardiology and 3 other medical specialty societies suggested that, in individuals with clinical or ECG features suggesting an arrhythmic syncope, ECG monitoring is indicated; the guidelines also stated that the “duration (and technology) of monitoring should be selected according to the risk and the predicted recurrence rate of syncope.”¹ Similarly, guidelines from the National Institute for Health and Care Excellence (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.² 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 1 to 2 weeks, an external event recorder is recommended; and if the frequency is less than once every 2 weeks, an implantable event recorder is recommended.

Similar to syncope, the evaluation and management of palpitations is patient-specific. In cases where the initial history, examination, and ECG findings are suggestive of an arrhythmia, some form of ambulatory ECG monitoring is indicated. A position paper from the European Heart Rhythm Association (2011) indicated that, for individuals with palpitations of unknown origin who have clinical features suggestive of arrhythmia, referral for specialized evaluation with consideration for ambulatory ECG monitoring is indicated.³

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 (eg, fatigue, malaise). It is classified as paroxysmal, persistent, or permanent based on symptom duration. Diagnosed AF may be treated with antiarrhythmic medications with the goal of rate or rhythm control. Other treatments include direct cardioversion, catheter-based radiofrequency- or cryo-energy-based ablation, or 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 was recommended by American Heart Association, American College of Cardiology, and Heart Rhythm Society in 2014 joint guidelines on patients with a history of stroke or transient ischemic attack.⁴

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

Patients with cryptogenic stroke are often monitored for the presence of AF because AF is estimated to be the cause of cryptogenic stroke in more than 10% of patients, and AF increases the risk of stroke.^{5,6} Paroxysmal AF confers an elevated risk of stroke, just as persistent and permanent AF 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 permits the evaluation of cardiac electrical activity over time, in contrast to a static ECG, which only permits the detection of abnormalities in cardiac electrical activity at a single point in time.

A Holter monitor is worn continuously and records cardiac electrical output continuously throughout the recording period. Holter monitors are capable of recording activity for 24 to 72 hours. 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 (eg, 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 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	Device Examples
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	<ul style="list-style-type: none"> • Zio® Event Card (iRhythm Technologies) • REKA E100™ (REKA Health)
Continuous recording devices with longer recording periods	Devices continuously worn and continuously record via ≥1 cardiac leads and store data longer than traditional Holter (14 d)	<ul style="list-style-type: none"> • Zio® Patch system (iRhythm Technologies)
External memory loop devices (patient- or autotriggered)	Devices continuously worn and store a single channel of ECG data in a refreshed memory. When the device is activated, the ECG is then recorded from the memory loop for the <i>preceding</i> 30-90 s and for next 60 s or so. 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).	<ul style="list-style-type: none"> • Patient-triggered: Explorer™ Looping Monitor (LifeWatch Services) • Autotriggered: LifeStar AF Express™ Auto-Detect Looping Monitor (LifeWatch Services) • Autotriggered or patient-triggered: King of Hearts Express® AF (Card Guard Scientific Survival)
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	<ul style="list-style-type: none"> • Autotriggered or patient-triggered: Reveal® XT ICM (Medtronic) • Autotriggered: BioMonitor, Biotronik)
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	<ul style="list-style-type: none"> • CardioNet MCOT (BioTelemetry) • LifeStar Mobile Cardiac Telemetry (LifeWatch Services) • SEEQ Mobile Cardiac Telemetry (Medtronic)

ECG: electrocardiogram.

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

REGULATORY STATUS

Some of the newer devices are described in the Background section for informational purposes. Because there may be many devices within each category, a comprehensive description of individual devices is beyond the scope of this review. U.S. Food and Drug Administration product codes include: DSH, DXH, DQK, DSI, MXD, MHX.

II. Criteria/Guidelines

A. The use of patient-activated or autoactivated external ambulatory event monitors (AEMs) OR continuous ambulatory monitors that record and store information for periods longer than 48 hours are covered (subject to Limitations and Administrative Guidelines) as a diagnostic alternative to Holter monitoring in the following situations:

1. Patients who experience infrequent symptoms (less frequently than every 48 hours) suggestive of cardiac arrhythmias (i.e., palpitations, dizziness, presyncope or syncope).
 2. Patients with atrial fibrillation (AF) who have been treated with catheter ablation, and in whom discontinuation of systemic anticoagulation is being considered.
 3. Patients with cryptogenic stroke who have a negative standard workup for AF including a 24-hour Holter monitor (see Policy Guidelines section).
- B. The use of implantable AEMs, either patient-activated or autoactivated, are covered (subject to Limitations and Administrative Guidelines) in the following situations:
1. In a small subset of patients who experience recurrent symptoms so infrequently that a prior trial of an external AEMs has been unsuccessful.
 2. In patients who require long-term monitoring for AF or possible AF (see Policy Guidelines section).

III. Policy Guidelines

The available evidence has suggested that long-term monitoring for atrial fibrillation postablation or after cryptogenic stroke is associated with improved outcomes, but the specific type of monitoring associated with the best outcomes is not well-defined. Trials demonstrating improved outcomes have used either event monitors or implantable monitors. In addition, there are individual patient considerations that may make 1 type of monitor preferable over another.

Therefore, for the evaluation of patients with cryptogenic stroke who have had a negative standard workup for atrial fibrillation including 24-hour Holter monitoring, or for the evaluation of atrial fibrillation after an ablation procedure, the use of long-term monitoring with an external event monitor, OR a continuous ambulatory monitor that records and stores information for periods longer than 48 hours, OR an implantable ambulatory monitor may be considered medically necessary for patients who meet the criteria outlined above.

IV. Limitations

- A. The use of outpatient cardiac telemetry (also known as mobile cardiac outpatient telemetry) as a diagnostic alternative to AEMs in patients who experience infrequent symptoms (less frequently than every 48 hours) suggestive of cardiac arrhythmias (i.e., palpitations, dizziness, presyncope, syncope) does not meet payment determination criteria.
- B. Other uses of AEMs, including outpatient cardiac telemetry and mobile applications, are not covered, including but not limited to the following situations because they are not known to be effective in improving health outcomes:
1. Monitoring asymptomatic patients with risk factors for arrhythmia.
 2. Monitoring effectiveness of antiarrhythmic medications.
 3. Detection of myocardial ischemia by detecting ST-segment changes.

V. Administrative Guidelines

- A. Precertification is required for implantable loop recorders. To precertify, please complete HMSA's **Precertification Request** and mail or fax the form, or use iExchange as indicated along with the following documentation:

1. Clinical documentation justifying the use of an implantable loop recorder.
 2. ECG results from a prior workup
 3. Documentation of a prior trial of an external AEM (if applicable)
- B. For services not requiring precertification, documentation supporting medical necessity must be kept in the patient’s medical records and be made available to HMSA upon request. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.
- C. Applicable codes:

CPT Codes	Description
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
0296T	; recording (includes connection and initial recording)
0297T	; scanning analysis with report
0298T	; review and interpretation
33286	Removal, subcutaneous cardiac rhythm monitor
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
93270	; recording (includes connection, recording, and disconnection)
93271	; transmission download and analysis
93272	; review and interpretation by a physician or other qualified health care professional

Codes for implantable cardiac monitoring devices (requires precertification)	
CPT Code	Description
33282	Implantation of patient-activated cardiac event recorder
33284	Removal of an implantable, patient-activated cardiac event recorder
33285	Insertion, subcutaneous cardiac rhythm monitor, including programming

- D. Codes that do not meet payment determination criteria:

CPT Codes	Description
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
0497T	External patient-activated, physician- or other qualified health care professional-prescribed, electrocardiographic rhythm derived event recorder without 24 hour attended monitoring; in-office connection
0498T	External patient-activated, physician- or other qualified health care professional-prescribed, electrocardiographic rhythm derived event recorder without 24 hour attended monitoring; review and interpretation by a physician or other qualified health care professional per 30 days with at least one patient-generated triggered event

VI. Scientific Background

This evidence review was created in July 1998 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through March 5, 2018.

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, 2 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 (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

This review is structured around 3 questions: First, in what clinical situations, and with what classes, do ambulatory event monitors (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 herein, including those that include real-time monitoring and analysis, the technologies represent an enhancement to existing technology and are intended to improve outcomes compared with event monitors. As such, to demonstrate an improvement in health outcomes, there must be a clinically significant incremental benefit when the additional technology, such as real-time monitoring, is added.

AEMS IN THE DETECTION OF ARRHYTHMIAS

The following 4 subsections focus 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 (eg, 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 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 (ELRs) have an established role in current clinical practice in evaluating suspected arrhythmias. A few pieces of evidence have suggested that autotriggered event monitors have an inherently higher yield than patient-activated AEMs. Several studies, including an analysis of a database of 100,000 patients, have compared the diagnostic yield of automatic and patient-activated arrhythmia recordings and reported an improved yield with autotriggering devices.⁷⁻⁹

Hoefman et al (2010) published a systematic review on diagnostic tools for detecting cardiac arrhythmias.¹⁰ 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 (ILRs). The yield varied among devices, with autotrigger devices providing the highest range of detection (72%-80%), followed by 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 2 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 more than 48 hours, either directly through comparison with Holter monitoring or indirectly through determination of the proportion of arrhythmias detected in the first 48 hours of monitoring.

Turakhia et al (2013) evaluated the diagnostic yield of the Zio Patch.¹¹ Data from the manufacturer were used to identify 26,751 first-time users of the device. The most common clinical indications were palpitations (40.3%), AF (24.3%), and syncope (15.1%). Mean duration of use was 7.6 days, and 95.9% of patients wore the device for more than 48 hours. At least 1 episode of arrhythmia was detected in 16,142 (60.3%) patients. The authors compared the detection rate in the first 48 hours with the detection rate over the entire time 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 (62.2%) with the first 48 hours (43.9%; $p < 0.001$). These data confirmed previous studies that had shown 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) compared arrhythmia detection rates in 146 patients who underwent simultaneous monitoring with a 24-hour Holter monitor and a 14-day Zio Patch monitor.¹² Included were patients referred for evaluation of a suspected cardiac arrhythmia at a single institution. For the detection of atrioventricular (AV) block, sinus pause, polymorphic ventricular tachycardia, supraventricular tachycardia (SVT), or AF, Holter monitoring detected 61 arrhythmias, while the Zio Patch detected 96 ($p < 0.001$). Over the monitoring period, the same 60 arrhythmia events were detected by both devices, with 36 only detected by the Zio Patch and 1 only detected by the Holter. 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 also suggested 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 might have clinical significance if its performance is similar in nonresearch settings.

Solomon et al (2016) evaluated the diagnostic yield for potentially high-risk arrhythmias during 14 days of continuous recording with the Zio Patch among 122,454 patients (122,815 recordings) included in a manufacturer registry.¹³ 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.

Bolourchi et al (2015) evaluated the diagnostic yield of 14 days of monitoring with the Zio Patch in a series of 3209 children included in a manufacturer registry.¹⁴ Patient age ranged from 1 month to 17 years. Indications for monitoring included palpitations (n=1138 [35.5%]), syncope (n=450 [14.0%]), unspecified tachycardia (n=291 [9.1%]), paroxysmal 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 referred for palpitations, 6.7% referred for syncope, 14.8% referred for tachycardia, 22.7% referred for paroxysmal SVT, and 6.5% referred for chest pain.

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.¹⁵ 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; 7 addressed long-term AEMs and 5 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	Population	Monitoring Indication	%	Main Findings
		Indication		
Eisenberg et al (2014) ¹⁶	524 consecutive patients evaluated in an academic EP practice	• Surveillance for unspecified arrhythmia or palpitations	47	<ul style="list-style-type: none"> • 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
		• Known/suspected AF	30	
		• Syncope	8	
		• Bradycardia surveillance	4	
		• Tachycardia surveillance	5	
		• Chest pain	2	
Schreiber et al	174 patients with symptoms	• Palpitations	44.8 24.1	<ul style="list-style-type: none"> • >1 significant arrhythmia other than chronic AF (≥4 beats VT, paroxysmal AF, ≥4 beats SVT, ≥3-s pause, 2nd-

(2014) ¹⁷	suggestive of arrhythmia seen in an ED	<ul style="list-style-type: none"> • Syncope • Unspecified arrhythmias detected in the ED 	11.5	degree Mobitz II or 3rd-degree AV block, or symptomatic bradycardia) detected in 83 (47.7%) <ul style="list-style-type: none"> • Median time to arrhythmia detection: <ul style="list-style-type: none"> ○ Any arrhythmia: 1.0 d (IQR, 0.2-2.8 d) ○ VT: 3.1 d ○ Sinus pause: 4.2 d ○ Significant heart block: 5.8 d
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AF: atrial fibrillation; AV: atrioventricular; ED: emergency department; EP: electrophysiology; IQR: interquartile range; SVT: supraventricular tachycardia; VT: ventricular tachycardia.

Section Summary: Diagnosis of Suspected Arrhythmias in Symptomatic Patients

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

AEMs and Patients With AF Treated With Catheter Ablation

Many patients with AF treated with catheter ablation are on long-term anticoagulation, and all patients treated with ablation are given anticoagulation for up to 3 months postprocedure. In patients with an apparently successful ablation who do not show signs or symptoms of recurrent AF at time periods longer than 3 months postablation, a decision whether to continue treatment with anticoagulants needs to be made. Studies have demonstrated that late recurrences are not uncommon after ablation and that these recurrent episodes are often asymptomatic.^{18,19} In addition, the presence of recurrent episodes of AF is a predictor of future thromboembolic events. In a larger observational study of 565 patients postablation, Chao et al (2011) found the 2 major predictors of thromboembolism were the CHADS2 score and the presence of recurrent episodes of AF.²⁰

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.²¹ Forty-four patients were enrolled and randomized; all patients received the ILR postablation. Six patients were excluded due to requests for device removal or loss to follow-up. During the first 6 months after ablation, all subjects underwent conventional monitoring that consisted of twice daily 1-minute pulse rate assessments by the patient and three 30-day transtelephonic monitoring periods. At 6 months postablation, patients were allocated to the randomization arm (on a 1:1 basis at initial enrollment) of either the ILR (transmission of data every 31 days) or conventional monitoring (twice daily 1-minute pulse rate assessment, 1 transtelephonic recording for 30 days at month 11). At 6 months postablation, conventional monitoring detected AF in 7 (18%) of 38 patients and the ILR confirmed AF in all of these patients. ILR monitoring also detected AF in an additional 11 (29%) patients. During the subsequent 6-month period, 5 of 18 patients in the conventional monitoring arm refused ongoing monitoring due to discomfort and

lifestyle restrictions; of the remaining 13, 5 (38%) had a recurrence of AF. In the ILR group, 5 (25%) of 20 patients had recurrence of AF. During the randomization period, 71% of patients in the ILR group discontinued their antiarrhythmic drugs compared with 44% in the conventional monitoring group over the randomization period ($p=0.04$).

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 for 3 months before and 18 months after ablation in 50 patients implanted with a cardiac monitor.²² Patients were instructed to keep a standardized diary record of arrhythmia symptoms. Based on diary reporting of symptoms, 29 (58%) of 50 patients were arrhythmia-free after ablation; based on recordings from 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, which included ambulatory monitoring, was negative for recurrent episodes. These patients appeared to have a low subsequent rate of thromboembolic events. In 1 study, Themistoclakis et al (2010) evaluated 3355 patients from 5 clinical centers, of whom 2692 discontinued anticoagulation at 3 to 6 months postablation and 663 continued anticoagulation medication.²³ During a mean follow-up of 28 months, 2 (0.07%) patients who discontinued anticoagulation experienced an ischemic stroke. This rate did not differ significantly from the stroke rate in patients who continued anticoagulation (0.45%). The rate of major hemorrhage was lower for patients who discontinued anticoagulation (2%) compared with those who continued (0.04%; $p<0.001$).

Section Summary: AEMs and Patients With AF Treated With Catheter 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 improve outcomes.

AEMs and Patients With Cryptogenic Stroke

Approximately 5% of patients with cryptogenic stroke will have AF diagnosed on ECG and/or telemetry monitoring in the hospital. The use of continuous telemetry monitoring has been compared with Holter monitoring for patients hospitalized for stroke or transient ischemic attack (TIA); these results are inconclusive as to which is the preferred method.^{24,25} Longer term ambulatory event monitoring will identify additional patients with asymptomatic episodes, with rates of detection estimated at 6% to 26% of patients.^{5,26,27}

Systematic Reviews

Sposato et al (2015) conducted a systematic review and meta-analysis of studies assessing rates of newly diagnosed AF after cryptogenic stroke or TIA based on cardiac monitoring, stratified into 4 sequential screening phases: phase 1 (emergency department) consisted of admission ECG; phase 2 (in-hospital) comprised serial ECG, continuous inpatient ECG monitoring, continuous inpatient cardiac telemetry, and in-hospital Holter monitoring; phase 3 (first ambulatory period) consisted of ambulatory Holter monitoring; and phase 4 (second ambulatory period) consisted of mobile cardiac outpatient telemetry (MCOT), external loop recording, and implantable loop recording.²⁸ In total, 50 studies with 11,658 patients met the inclusion criteria. Studies were mixed in their patient composition: 22 (28%) included only cryptogenic stroke cases, 4 (5%) stratified events into cryptogenic and noncryptogenic, and 53 (67%) included unselected patient populations. The proportion of patients diagnosed with poststroke AF during the ambulatory phases was 10.7% (95% CI, 5.6% to 17.2%) in phase 3, and 16.9% (95% CI, 13.0% to 21.2%) in phase 4. The overall AF detection yield after all phases of sequential cardiac monitoring was 23.7% (95% CI, 17.2% to 31.0%). In phase 4, there were no differences between the proportion of patients diagnosed with 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%), or ILR (16.9%; 95% CI, 10.3% to 24.9%; $p=0.97$).

Kishore et al (2014) conducted a systematic review and meta-analysis of prospective observational studies and RCTs that have reported detection rates of newly diagnosed AF in patients with ischemic stroke or TIA who had had any cardiac monitoring for at least 12 hours.²⁹ Thirty-two studies were selected: 18 studies included patients with ischemic stroke only, 1 study included TIA only, and 13 studies included both ischemic stroke and TIA. Reviewers reported significant study heterogeneity. Among unselected patients (ie, selected on the basis of stroke pathogenesis, age, or prescreening for AF), the detection rate of any new AF was 6.2% (95% CI, 4.4% to 8.3%); among selected patients, it was 13.4% (95% CI, 9.0% to 18.4%). In cryptogenic strokes, new AF was detected in 15.9% of patients (95% CI, 10.9% to 21.6%). Among selected patients, the AF detection rate during 24-hour Holter monitoring was 10.7% (95% CI, 3.4% to 21.5%), while the detection rate during monitoring beyond 24 hours (including more prolonged Holter monitoring, implantable and nonimplantable loop recording, and MCOT) was 14.7% (95% CI, 10.7% to 19.3%).

The Kishore study and others suggest that longer periods of cardiac monitoring increase the likelihood of AF detection. However, many of these asymptomatic episodes of AF are brief and their relation to the preceding stroke uncertain, because 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

Four RCTs were identified that evaluated ambulatory monitoring in patients with cryptogenic stroke. Two were small pilot trials. One small pilot RCT published by Kamel et al (2013) randomized

40 patients with cryptogenic ischemic stroke or high-risk TIA to usual care or to 21 days of MCOT (see Table 3).³⁰ There were no cases of AF detected in either group (see Table 4). Two patients in the MCOT group had nonsustained ventricular tachycardia detected, which was of uncertain clinical significance in relation to their strokes.

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).³¹ Sustained AF (recorded for the complete 20-second rhythm strip after event triggering) was detected significantly more often with the ELR than with standard care at 14-day follow-up. The difference did not differ statistically at 90-day follow-up (see Table 4).

Sanna et al (2014) reported on results from the CRYSTAL AF trial, an RCT that evaluated whether long-term monitoring with implantable cardiac monitors in patients who had cryptogenic stroke would lead to changes in anticoagulant management and/or improved outcomes (see Table 3).^{32,33} The trial randomized 441 patients to continuous monitoring with the Reveal XT ICM or routine care. Eligibility criteria included no known history of AF, cryptogenic stroke, or TIA with infarct, and no mechanism determined after a workup that included 12-lead ECG, 24-hour Holter monitoring, transesophageal echocardiography, 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 patients randomized, 416 (94.3%) completed 6-month follow-up, 2 were lost to follow-up, 5 died, and 18 exited the trial before 6 months. Crossover occurred in 12 patients in the ICM group and 6 in the control group. AF was detected in 8.9% of the ICM group compared with 1.4% of the control group (hazard ratio [HR], 6.43; 95% CI, 1.90 to 21.74) (see Table 4). Median time from randomization to detection of AF was 41 days (interquartile range, 14-84 days) in the ICM group and 32 days (interquartile range, 2-73 days) in the control group. Most AF episodes in the ICM group were asymptomatic (74%) compared with 33% in the control group. The rate of AF detection was similarly greater in the ICM group at the 12-month follow-up (see Table 4). Use of oral anticoagulants was 10.1% in the implantable cardiac monitoring group and 4.6% in the control group at 6 months ($p=0.04$) and 14.7% and 6.0% at 12 months ($p=0.007$), respectively. Five (2.4%) of the 208 implantable cardiac monitors inserted were removed due to infection or erosion of the device pocket.

Brachmann et al (2016) reported on 3-year follow-up results from the CRYSTAL AF trial.³⁴ At trial closure, 48 subjects had completed 3 years of follow-up ($n=24$ in each treatment group). By 3 years, the HR for detecting AF for ICM-monitored vs control patients was 8.8 (95% CI, 3.5 to 22.2; $p<0.001$).

Gladstone et al (2014) reported on results from the EMBRACE study, an RCT that compared 30-day autotriggered external loop cardiac event monitors with conventional 24-hour monitors for the detection of AF in patients with cryptogenic stroke (see Table 3).³⁵ Included patients were ages 55 years or older, with no known history of AF, and an ischemic stroke or TIA of undetermined cause

within the prior 6 months. All patients underwent standard screening for AF with 1 or more ECGs and 1 or more 24-hour Holter monitors. In total, 572 patients were randomized to an ELR (ER910AF Cardiac Event Monitor, Braemar) or to a 24-hour Holter monitor. Among intervention group subjects, 82% completed at least 3 weeks of monitoring. AF was detected in 45 (16.1%) of 280 patients in the intervention group compared with 9 (3.2%) of 277 patients in the control group (risk difference, 12.9 percentage points; 95% CI, 8.0 to 17.6; $p < 0.001$) (see Table 4). At 90-day follow-up, patients in the intervention group (18.6%) were more likely to be treated with anticoagulants than those in the control group (11.1%; absolute treatment difference, 7.5 percentage points; 95% CI, 1.6 to 13.3; $p = 0.01$).

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

					Interventions (n)	
Study	Country	Sites	Dates	Participants	Active	Comparator
Kamel et al (2013) ³⁰	U.S.	1	2009-2011	Cryptogenic ischemic stroke or high-risk TIA	MCOT (20)	Standard (20)
Higgins et al (2013) ³¹	U.K.	2	2010-2011	Transient or persistent symptoms of acute TIA	ELR (50)	Standard (50)
Sanna et al (2014) ³³ & Brachmann et al (2016) ³⁴	Canada, Europe, U.S.	55	2009-2012	Cryptogenic ischemic stroke or TIA	ILR (221)	Standard (220)
Gladstone et al (2014) ³⁵	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) ³⁰	90 d	0	0	NS	<ul style="list-style-type: none"> 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) ³¹	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) ³³ ; Brachmann et al (2016) ³⁴	6 mo 12 mo 3 y	8.9 12.4 30	1.4 2.0 3.0	<0.001 <0.001 <0.001	<ul style="list-style-type: none"> 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) ³⁵	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 noncomparative studies published before the RCTs described above have reported on AF detection rates after cryptogenic stroke and long-term monitoring with various devices, including ILRs,^{6,36,37} and continuous monitors with longer recording periods,³⁸ along with a pilot study evaluating the Zio Patch for AF detection poststroke.³⁹

Section Summary: AEMs and Patients With Cryptogenic Stroke

Randomized studies, including 2 large RCTs, have demonstrated that long-term monitoring is associated with higher rates of AF detection than Holter monitors 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 Asymptomatic Patients

Screening for AF in asymptomatic patients has been proposed to reduce burden of stroke. Evaluating the net benefit of screening for AF in asymptomatic patients requires considering: risk of stroke in absence of screening; incremental benefit of earlier vs later treatment for stroke when AF is detected; and potential harms of overdiagnosis.

Assessing the prevalence of asymptomatic AF is difficult because of the lack of symptoms. Approximately a third of all patients with AF are estimated to be asymptomatic.⁴⁰ Studies have suggested that most paroxysmal episodes of AF are asymptomatic.^{41,42} It is uncertain whether patients with paroxysmal AF have a stroke risk comparable to those with persistent or permanent AF; some studies have suggested the risk of stroke is similar^{43,44} while in a systematic review of 12 studies (total N=99,996 patients), Ganesan et al (2016) found that the risks of thromboembolism and all-cause mortality were higher with nonparoxysmal than with paroxysmal AF.⁴⁵ 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 increased bleeding risk.

Screening for AF in asymptomatic patients could be either systematic or targeted to high-risk populations. European guidelines for screening for AF are based on a large-cluster RCT (Fitzmaurice et al [2007]; N=14,802) of opportunistic pulse taking vs systematic screening with 12-lead ECG or standard care in general practice.⁴⁶ This RCT 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).⁴⁷ Patients were 65 years and older, asymptomatic, with CHA₂DS₂-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

Turakhia et al (2015) reported on results for a single-center noncomparative study evaluating the feasibility and diagnostic yield of a continuous recording device with longer recording period (Zio Patch) for patients with risk factors for AF.⁴⁸ The study included 75 patients older than age 55 with at least 2 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 (97%) were considered at moderate to high risk of stroke (CHA2DS2-VASc scores ≥ 2). After a mean follow-up of 7.6 days, AF was detected in 4 (5.3%) subjects, all of whom had CHA2DS2-VASc scores of 2 or greater. All patients with AF detected had an initial episode within the first 48 hours of monitoring. Five patients had detected episodes of atrial tachyarrhythmias lasting at least 60 seconds.

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.⁴⁹ 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: AEMs for AF Detection in Asymptomatic Patients

For the use of ambulatory monitoring in the diagnosis of AF in asymptomatic but higher risk patients, a small noncomparative 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 1 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 those 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 or 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 and that an ILR as an initial strategy may be reasonable.

ILR Use for Individuals With Signs and/or 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.⁵⁰ 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%; I²=80%). Diagnoses included arrhythmic syncope, ventricular arrhythmia, supraventricular arrhythmia, and bradyarrhythmia. Reviewers noted that an important analytic limitation was the considerable heterogeneity among studies, partly because definitions of syncope and methods to assess unexplained syncope were inconsistent.

Burkowitz et al (2016) conducted a systematic review and meta-analysis of ILRs in the diagnosis of syncope and the detection of AF.⁵¹ For syncope diagnosis, the review identified 3 RCTs comparing ILRs with a conventional diagnosis strategy (Holter monitoring). In pooled analysis, an ILR diagnosis strategy was associated with a higher likelihood of the end point of diagnostic yield (relative risk, 4.17; 95% CI, 2.57 to 6.77; I²=14%). The RCTs (Da Costa et al [2013],⁵² Farwell et al [2004],⁵³ and Krahn et al [2001]⁵⁴) are described below.

Randomized Controlled Trials

Podoleanu et al (2014) reported on results of an open-label RCT comparing 2 strategies for evaluating syncope—an experimental strategy involving the early use of an ILR and a conventional evaluation strategy excluding an ILR (see Table 5).⁵⁵ The trial included patients who had a single syncope (if severe and recent) or at least 2 syncopes in the past 12 months. The syncope had to be unexplained at the end of clinical examination and who had a workup with 12-lead ECG, echocardiography, and head-up tilt-test. Patients randomized to ILR received the Reveal or Reveal Plus device. After 14 months of follow-up, a definitive cause of syncope was established more frequently in the ILR group than in the standard care group (see Table 6). Arrhythmic causes of syncope in the ILR group included 2 (5%) cases of AV block, 4 (10%) cases of sinus node disease, 1 (2.5%) case of AF, 1 (2.5%) case of ventricular fibrillation, and 3 (8%) other tachycardias. In the conventionally managed group, 8 patients had a diagnosis of presumed reflex syncope.

A small RCT by Da Costa et al (2013) compared use of an ILR with a conventional follow-up strategy in 78 patients with a first episode of syncope (see Table 5).⁵² A significant number of patients had cardiomyopathy (23%), AF (15.4%), and/or bundle branch block (58%) on ECG. Twenty-one (27%) patients had at least 1 arrhythmia detected, with a significant difference in the detection rate for the ILR group compared with the conventional follow-up group (see Table 6).

Giada et al (2007) conducted an RCT assessing 2 diagnostic strategies in 50 patients with infrequent (≤ 1 episode per month) unexplained palpitations—an ILR strategy (n=26) and a conventional strategy (n=24) including 24-hour 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).⁵⁶ Prior cardiac evaluation in eligible patients included standard ECG and echocardiography. Rhythm monitoring was considered diagnostic when a symptom-rhythm correlation was demonstrated during spontaneous palpitations that resembled pre-enrollment symptoms. In the conventional strategy group, a diagnosis was made in 5 (21%) subjects, after a mean time to diagnosis of 36 days, based on external ECG monitoring in 2 subjects and electrophysiologic studies in 3 subjects. In the ILR group, a diagnosis was made in 19 subjects after a mean time to diagnosis of 279 days (see Table 6).

Farwell et al (2004) reported on an RCT comparing the diagnostic yield of an ILR (Reveal Plus) with a conventional diagnostic strategy in 201 patients with unexplained syncope (see Table 5).⁵³ Eligible patients were evaluated at a single institution for recurrent syncope and had no definitive diagnosis after a basic initial workup (including 12-lead ECG, Holter monitoring in patients with suspected cardiac syncope, upright cardiac sinus massage, and tilt-table testing). At last follow-up, more loop recorder patients had an ECG diagnosis than control patients (HR for ECG diagnosis, 8.93; 95% CI, 3.17 to 25.19; $p < 0.001$) (see Table 6). Seven of the loop recorder patients were diagnosed 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.

An earlier RCT by Krahn et al (2001) compared a conventional monitoring strategy (ELR monitoring for 2-4 weeks, followed by tilt-table and electrophysiologic testing) with at least 1 year of monitoring using an ILR in 60 subjects with unexplained syncope (n=30 per group) (see Table 5).⁵⁴ Eligible patients had a previous clinical assessment, at least 24 hours of continuous ambulatory monitoring or inpatient telemetry, and a transthoracic echocardiogram. A diagnosis was made in 20% of those in the conventional monitoring arm and in 52% of those in the ILR arm (see Table 6).

Table 5. Summary of RCT Characteristics for ILRs for Arrhythmia

Study	Country	Sites	Dates	Participants	Active	Comparator
Podoleanu et al (2014) ⁵⁵	France	13	2004-2008	Single recent syncope or 2 in past 12 mo	ILR (39)	Standard (39)
Da Costa et al (2013) ⁵²	France	Multiple, NS	2005-2010	Single syncope	ILR (41)	Standard (37)
Giada et al (2007) ⁵⁶	Italy	Multiple, NS	NR	Unexplained palpitations	ILR (26)	Standard (24)
Farwell et al (2004) ⁵³	England	1	2000-2001	≥ 2 unexplained syncope in past 12 mo	ILR (103)	Standard (98)
Krahn et al (2001) ⁵⁴	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, n (%)			Additional Findings
		ILR	Standard	p	
Podoleanu et al (2014) ⁵⁵	14 mo	18 (46)	2 (5)	<0.001	<ul style="list-style-type: none"> Advanced cardiology tests performed less frequently in ILR group vs standard (p=0.05) No difference in QOL
Da Costa et al (2013) ⁵²	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) ⁵⁶	≥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) ⁵³	≥6 mo	34 (33)	4 (4)	<0.001	<ul style="list-style-type: none"> ECG-directed therapy was initiated quicker in the ILR group No difference in syncopal episodes, mortality, or QOL
Krahn et al (2001) ⁵⁴	12 mo	14 (52)	6 (20)	0.012	<ul style="list-style-type: none"> 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 ILR (the Reveal Plus, DX, or XT device) because of unexplained syncope, Edvardsson et al (2014) described the monitoring yield in 570 patients implanted and followed for at least a year or until diagnosis.⁵⁷ Most (97.5%) patients had a standard ECG before initiation of the ILR, 11.8% had prior ELR, and 54.6% had in-hospital ECG monitoring. During the monitoring period, 218 (38%) patients had recurrent syncope. The proportion of specific diagnoses based on the ILR is not reported, but of subjects who had a recurrence, 42.2% had a pacemaker implanted, 4.6% had an implantable cardioverter defibrillator placed, 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.⁵⁸

ILRs in the Detection of AF

As noted above in the discussion of AEMs for the detection of AF, some trials have demonstrated improved outcomes with monitoring strategies (ie, the CRYSTAL AF) that used ILRs. Autotrigger ILRs have also been developed specifically to detect AF through the use of detection algorithms. Several nonrandomized studies have evaluated the accuracy of autotriggered ILRs for the diagnosis of AF.

Systematic Reviews

Afzal et al (2015) reported on a systematic review and meta-analysis of studies comparing ILRs with wearable AEMs for prolonged outpatient rhythm monitoring after cryptogenic stroke.⁵⁹ Reviewers included 16 studies (total N=1770 patients) 3 RCTs and 13 observational studies. For ILR-monitored patients, the median monitoring duration was 365 days (range, 50-569 days), while for wearable device-monitored patients, the median monitoring duration was 14 days (range, 4-30 days). Compared with wearable 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, a single RCT and 5 noncomparative studies met inclusion criteria.⁵¹ The sole RCT identified was that by Sanna et al, described in the cryptogenic stroke indication.³³

Observational Studies

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).⁶⁰ 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.

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.⁶¹ 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.⁶² This nonrandomized, prospective trial 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%, respectively.

Ziegler et al (2015) reported on a large (N=1247) set of patients identified from the manufacturer's registry undergoing ILR monitoring for AF detection after a cryptogenic stroke.⁶³ Over a median follow-up of 182 days, 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 the CRYSTAL AF trial.

Hindricks et al (2010) evaluated the accuracy of an autotriggered ILR in 247 patients at high risk for paroxysmal AF.⁶⁴ 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 AF episodes of 2 or more minutes was 88.2%, increasing to 92.1% for episodes of 6 or more minutes. AF was falsely identified by the loop recorder in 19 of 130 patients who did not have AF while on a Holter monitor, for a false-positive rate of 15%. AF burden was accurately measured by the loop recorder, with the mean absolute difference between the loop recorder and Holter monitor of 1.4%.

Hanke et al (2009) compared an autotrigger ILR with 24-hour Holter monitoring done at 3-month intervals in 45 patients who had undergone surgical ablation for AF.⁶⁵ After a mean follow-up of 8.3 months, the ILR identified AF in 19 (42%) patients in whom Holter monitoring recorded sinus rhythm.

Safety of ILRs

Mittal et al (2015) reported on safety outcomes related to the use of an ILR, based on data from 2 studies, the Reveal LINQ Usability study and the Reveal LINQ Registry.⁶⁶ 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 is inserted with a preloaded insertion tool via a small skin incision. In the Usability study, 1 serious adverse event was recorded (insertion site pain); in the Registry study, 2 serious adverse events were recorded (1 case each of insertion site pain and insertion site infection). The rates of infection and procedure-related serious adverse events in the Usability study were 1.3% and 0.7%, respectively, and 1.6% and 1.6%, respectively, in the Registry study.

Section Summary: Implantable Loop Recorders

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 MCOT to ambulatory cardiac monitoring 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 (eg, 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

An RCT by Rothman et al (2007) compared MCOT with standard event monitors.⁶⁷ This trial involved 305 patients randomized to the LOOP recorder or to MCOT (CardioNet) and monitored for up to 30 days. The unblinded study at 17 centers enrolled patients with symptoms of syncope, presyncope, or severe palpitations occurring less frequently than once per 24 hours and a nondiagnostic 24-hour Holter or telemetry monitor within the prior 45 days. Test results were read by an electrophysiologist blinded to the monitoring device assignment. Most patients in the control group had a patient-triggered event monitor. Only a subset of patients (n=50) had autotrigger devices, thus precluding comparison between MCOT and autotrigger devices. Of the 305 patients, 266 completed at least 25 days of monitoring. A diagnostic end point (confirmation or 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, symptoms consisting of rapid AF and/or flutter (15 patients vs 1 patient), and ventricular tachycardia defined as more than 3 beats and rate greater than 100 (14 patients vs 2 patients). These differences were thought to be clinically significant rhythm disturbances and the likely causes of the patients' symptoms. The trialists did not comment on the clinical impact (changes in management) of these findings in patients for whom the rhythm disturbance did not occur simultaneously with symptoms. In this trial, median time to diagnosis in the total study population was 7 days in the MCOT group and 9 days in the LOOP group.

Observational Studies

Arrhythmia Detection

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).⁶⁸ 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.

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.⁶⁹ Medical records from 26,438 patients who had undergone MCOT during a 9-month

period from a single service provider were retrospectively examined. During a mean monitoring period of 21 days, 21% (5459) had an arrhythmic event requiring physician notification. Of these, 1% (260) had an event that could be considered potentially emergent. These potentially emergent events included 120 patients with wide-complex tachycardia, 100 patients with sinus pauses 6 seconds or longer, and 42 with sustained bradycardia at less than 30 beats per minute.

A number of uncontrolled case series have reported on arrhythmia detection rates of MCOT.⁷⁰⁻⁷³ One study (Joshi et al [2005]) described the outcomes of a consecutive case series of 100 patients.⁷⁰ Included patients had the following symptoms: palpitations (47%), dizziness (24%), or syncope (19%). Patients being evaluated for the efficacy of drug treatment (25%) were also included. Clinically significant arrhythmias were detected in 51% of patients, but half of these patients were asymptomatic. The authors commented that the automatic detection resulted in an increased diagnostic yield, but there was no discussion of its unique features (ie, the real-time analysis, transmission, and notification of arrhythmia).

AF Detection

In the largest study evaluating the diagnostic yield of MCOT for AF, Favilla et al (2015) evaluated a retrospective cohort of 227 patients with cryptogenic stroke or TIA who underwent 28 days of monitoring with MCOT.⁷⁴ AF was detected in 14% (31/227) of patients, of whom 3 reported symptoms at the time of AF. Oral anticoagulation was initiated in 26 (84%) patients diagnosed with AF. Of the remaining 5 (16%) not on anticoagulation therapy, 1 had a prior history of gastrointestinal bleeding, 3 were unwilling to accept the risk of bleeding, and 1 failed to follow up.

Miller et al (2013) retrospectively analyzed paroxysmal AF detection rates among 156 patients evaluated with MCOT within 6 months of a cryptogenic stroke or TIA.²⁷ Over a median 21-day period of MCOT monitoring (range, 1-30 days), AF was detected in 17.3% of patients. Mean time to first occurrence of AF was 9 days (range, 1-21 days).

In an uncontrolled case series, Tayal et al (2008) retrospectively analyzed patients with cryptogenic stroke who had not been diagnosed with AF by standard monitoring.⁷³ In this study, 13 (23%) of 56 patients with cryptogenic stroke had AF detected by MCOT. Twenty-seven asymptomatic AF episodes were detected in the 13 patients; 23 of them were less than 30 seconds in duration. In contrast, Kalani et al (2015) reported a diagnostic yield for AF of 4.7% (95% CI, 1.5% to 11.9%) in a series of 85 patients with cryptogenic stroke.⁷⁵ In this series, 82.4% of patients had completed transesophageal echocardiography, cardiac magnetic resonance imaging, or both, with negative results. Three devices were used and described as MCOT devices: 34% received LifeStar ACT ambulatory cardiac telemetry, 41% received the LifeStar AF Express autodetect looping monitor, and 25% received the Cardiomedix cardiac event monitor. While the authors reported that there was a system in place to transmit the data for review, it is unclear whether data were sent in “real-time.”

Section Summary: Mobile Cardiac Outpatient Telemetry

The available evidence has suggested that MCOT is likely to be 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, permitting for emergent intervention for potentially life-threatening arrhythmias. One study reported that 1% of arrhythmic events detected on MCOT during a mean monitoring period of 21 days per patient could be considered potentially emergent. However, no studies were identified that addressed whether the use of 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. Currently, the evidence does not demonstrate a clinically significant incremental benefit for MCOT.

SUMMARY OF EVIDENCE

Ambulatory Event Monitoring

For individuals who have signs and/or symptoms suggestive of arrhythmia(s) who receive patient- or autoactivated 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 detects more arrhythmias than 24- or 48-hour Holter monitoring. Particularly for patients who, without the more prolonged monitoring, would 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 who have AF following ablation who receive long-term ambulatory cardiac monitoring, the evidence includes an RCT comparing ambulatory event monitoring with standard care and several observational studies. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. The RCT evaluating a long-term monitoring strategy after catheter ablation for AF reported significantly higher rates of AF detection. The available evidence has suggested that long-term monitoring for AF postablation is associated with improved outcomes. However, 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 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 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 are asymptomatic with risk factors for AF who receive long-term ambulatory cardiac monitoring, the evidence includes an RCT and 2 nonrandomized 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 1 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

For individuals who have signs and/or symptoms suggestive of arrhythmia with infrequent symptoms who receive patient- or autoactivated implantable ambulatory event monitoring, the evidence includes RCTs comparing implantable loop recorders with shorter term monitoring, usually 24- to 48-hour Holter monitoring. Relevant outcomes are overall survival, morbid events, medication use, and treatment-related morbidity. Studies assessing prolonged implantable loop recorders in patients have reported high rates of arrhythmia detection compared with shorter external event or Holter monitoring. These studies have supported use of a progression in diagnostics from an external event monitor to implantable loop recorder 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 who have signs and/or symptoms suggestive of arrhythmia who receive outpatient cardiac telemetry, the evidence includes an RCT and nonrandomized studies evaluating rates of arrhythmia detection using 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.

SUPPLEMENTAL INFORMATION

CLINICAL INPUT FROM PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2014 Input

In response to requests, input was received from 3 physician specialty societies and 4 academic medical centers (3 reviews) while this policy was under review in 2014. Input was obtained to provide information on mobile cardiac outpatient telemetry and new devices. There was no consensus whether mobile cardiac outpatient telemetry is medically necessary. While reviewers agreed that mobile cardiac outpatient telemetry is comparable to event monitors for arrhythmia detection, they did not agree on whether the real-time monitoring provides incremental benefit over external event monitors or is associated with improved health outcomes compared with external event monitors. There was consensus on the medical necessity of externally worn event monitors with longer continuous recording periods as an alternative to Holter monitors or event monitors. For implantable memory loop devices that are smaller than older-generation devices, there was consensus that these devices improve the likelihood of obtaining clinically useful information due to improved ease of use, but there was no consensus that such devices improve clinical outcomes and are medically necessary.

2009 Input

In response to requests, input was received from 1 physician specialty society and 4 academic medical centers (5 reviews) while this policy was under review in 2009. There were differences among reviewers on outpatient cardiac telemetry, with some reviewers concluding it had a role in certain subsets of patients (eg, in those with sporadic atrial fibrillation). Other reviewers commented that the value of this technology should be considered in both providing a diagnosis and in making treatment decisions. At times, excluding arrhythmia as a cause of a patient's symptoms is an important finding.

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.⁷⁶ Below are 2 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	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Long-term recording of ≥14 d Excellent patient acceptance 	<ul style="list-style-type: none"> Limited ECG from closely spaced electrodes, lacking localization of arrhythmia origin Inconsistent ECG quality due to body type variations
External loop recorders	<ul style="list-style-type: none"> Records only selected ECG segments marked as events either automatically or manually by patient Immediate alarm generation on event detection 	<ul style="list-style-type: none"> Single-lead ECG, lacking localization of arrhythmia origin Cannot continuously document cardiac rhythm Requires patient to wear electrodes continuously
Event recorders	<ul style="list-style-type: none"> Records only selected ECG segments after an event is detected by patient Immediate alarm generation at event detected by patient Well-tolerated by patient 	<ul style="list-style-type: none"> Single-lead ECG, lacking localization of arrhythmia origin Cannot continuously document cardiac rhythm Diagnostic yield dependent on patient ability to recognize correct symptom
Mobile cardiac telemetry	<ul style="list-style-type: none"> Multilead, so higher sensitivity and specificity of arrhythmia detection Streams data continuously; can be programmed to autodetect and autosend events at prescribed time intervals Immediate alarm generation on event without patient interaction 	<ul style="list-style-type: none"> 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	!	B-NR
Specific conditions for use of ambulatory ECG		
Unexplained syncope, when tachycardia suspected	I	B-R
Unexplained palpitation	I	B-R
Detection of atrial fibrillation, triggering arrhythmias, and postconversion pauses	IIa	B-NR
Cryptogenic stroke, to detect undiagnosed atrial fibrillation	I	B-R

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.

In 2014, the American College of Cardiology, the American Heart Association, and HRS issued guidelines on the management of patients with atrial fibrillation (AF).⁴ These guidelines recommended the use of Holter or event monitoring if the diagnosis of the type of arrhythmia is in question or as a means of evaluating rate control.

The 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 mobile cardiac outpatient telemetry.	Ila	B-NR
To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, an implantable cardiac monitor can be useful.	Ila	B-R

COR: class of recommendation; LOE: level of evidence.

a COR definitions: I: strong recommendation; Ila: 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	<ul style="list-style-type: none"> • Frequent spontaneous symptoms likely within 2 to 6 wk • Limited use when syncope associated with sudden incapacitation
External loop recorder (patient or auto-triggered)	Frequent spontaneous symptoms likely to occur within 2 to 6 wk
External patch recorder	<ul style="list-style-type: none"> • Alternative to external loop recorder • Leadless, so more comfortable, resulting in improved compliance • Offers only 1-lead recording
Mobile cardiac outpatient telemetry	<ul style="list-style-type: none"> • 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 2 indications, unexplained syncope and unexplained recurrent palpitations, but did not explicitly distinguish between continuous (ie, Holter monitoring) and intermittent (ie, ambulatory event monitoring) monitoring. Regarding the effectiveness of antiarrhythmic therapy, the guidelines listed 1 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 (AEMs) 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 et al

A consensus document on catheter and surgical ablation for AF was published in 2012 by HRS, the European Heart Rhythm Association, and the European Cardiac Arrhythmia Society⁷⁹ and updated in 2017.⁸⁰ This document did not contain formal practice guidelines, but provided general recommendations based on literature review and expert consensus. Use of ambulatory event monitors postablation was addressed in 2 sections of the document. First, in the section discussing use of anticoagulation following ablation, the following statement was made:

“Patients in whom discontinuation of systematic anticoagulation is being considered based on patient values and preferences should consider undergoing continuous or frequent ECG [electrocardiogram] monitoring to screen for AF recurrence.”

In the section on postoperative rhythm monitoring of patients who are postablation, 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, the European Heart Rhythm Association published guidelines on the use of diagnostic implantable and external loop recorders.⁸¹ For the indications that the Association considered established at the time of publication, the guidelines made the following statements about indications for implantable and external recorders (see Table 11).

Table 11. Guidelines on Use of Diagnostic ILRs and ELRs

Recommendation	COR	LOE
“ILR [implantable loop recorder] is indicated: <ul style="list-style-type: none"> • “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 	I	A

• “a likely recurrence within battery longevity of the device.”		
“ELRs 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.”	I	B
“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.”	Ila	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.”	Ila	B
“ELRs [external loop recorder] may be indicated in patients with recurrent (pre)syncope who have: <ul style="list-style-type: none"> • “inter-symptom interval of ≤4 weeks, and • “suspicion of arrhythmic origin and • “absence of high-risk criteria that require immediate hospitalization or intensive evaluation....” 	Ila	B

COR: class of recommendations; ECG: electrocardiogram; ELR: external loop recorder; ILR: implantable loop recorder; LOE: level of evidence.

American Academy of Neurology

In 2014, the American Academy of Neurology updated its guidelines on the prevention of stroke in patients with nonvalvular AF (NVAf).⁸² These guidelines made the following recommendations on the identification of patients with occult NVAf:

A1. “Clinicians might obtain outpatient cardiac rhythm studies in patients with cryptogenic stroke without known NVAf, to identify patients with occult NVAf (Level C).

A2. Clinicians might obtain cardiac rhythm studies for prolonged periods (e.g., for 1 or more weeks) instead of shorter periods (e.g., 24 hours) in patients with cryptogenic stroke without known NVAf, to increase the yield of identification of patients with occult NVAf (Level C).”

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable.

MEDICARE NATIONAL COVERAGE

The Centers for Medicare & Medicaid Services implemented a national coverage determination in 2004 for electrocardiographic services.⁸³ This national coverage determination includes descriptions of the Holter monitor and event recorders (both external loop recorders and implantable loop recorders). Ambulatory cardiac monitors are covered when there is documentation of medical necessity. Indications for use include detection of symptomatic transient arrhythmias and determination of arrhythmic drug therapy (to either initiate, revise, or discontinue the therapy).

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently unpublished trials that might influence this review are listed in Table 12.

Table 12. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02392754	Home-Based Screening for Early Detection of Atrial Fibrillation in Primary Care Patients Aged 75 Years and Older (SCREEN-AF)	822	Dec 2018
NCT02786940	Remote Cardiac Monitoring of Higher-Risk Emergency Department Syncope Patients after Discharge (REMOSYNC)	600	May 2019
NCT03001765	Impact of an Intensive Monitoring Strategy in Symptomatic Patients with Suspected Arrhythmia (IMPACT)	150	Jul 2019
NCT02428140 ^a	Post-Embolism Rhythm Detection With Implantable Versus External Monitoring (PERDIEM)	300	Dec 2019
NCT02793895	Detection of Atrial Fibrillation After Cardiac Surgery (SEARCH-AF)	396	Sep 2020
NCT02684825	Detection of Silent Atrial Fibrillation after Ischemic Stroke (SAFFO)	424	Jun 2021

^a Denotes industry involvement

NCT: national clinical trial.

VII. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii's Patients' Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VIII. References

1. Task Force for the Diagnosis Management of Syncope, European Society of Cardiology, European Heart Rhythm Association, et al. Guidelines for the diagnosis and management of syncope (version 2009). *Eur Heart J*. Nov 2009;30(21):2631-2671. PMID 19713422
2. National Institute for Health and Care Excellence (NICE). Transient loss of consciousness ('blackouts') in over 16s [CG109]. 2014; <https://www.nice.org.uk/guidance/cg109>. Accessed March 15, 2018.
3. Raviele A, Giada F, Bergfeldt L, et al. Management of patients with palpitations: a position paper from the European Heart Rhythm Association. *Europace*. Jul 2011;13(7):920-934. PMID 21697315
4. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of

- Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation*. Dec 2 2014;130(23):2071-2104. PMID 24682348
5. Mittal S, Movsowitz C, Steinberg JS. Ambulatory external electrocardiographic monitoring: focus on atrial fibrillation. *J Am Coll Cardiol*. Oct 18 2011;58(17):1741-1749. PMID 21996384
 6. Christensen LM, Krieger DW, Hojberg S, et al. Paroxysmal atrial fibrillation occurs often in cryptogenic ischaemic stroke. Final results from the SURPRISE study. *Eur J Neurol*. Jun 2014;21(6):884-889. PMID 24628954
 7. Balmelli N, Naegeli B, Bertel O. Diagnostic yield of automatic and patient-triggered ambulatory cardiac event recording in the evaluation of patients with palpitations, dizziness, or syncope. *Clin Cardiol*. Apr 2003;26(4):173-176. PMID 12708623
 8. Ermis C, Zhu AX, Pham S, et al. Comparison of automatic and patient-activated arrhythmia recordings by implantable loop recorders in the evaluation of syncope. *Am J Cardiol*. Oct 1 2003;92(7):815-819. PMID 14516882
 9. Reiffel JA, Schwarzberg R, Murry M. Comparison of autotriggered memory loop recorders versus standard loop recorders versus 24-hour Holter monitors for arrhythmia detection. *Am J Cardiol*. May 1 2005;95(9):1055-1059. PMID 15842970
 10. Hoefman E, Bindels PJ, van Weert HC. Efficacy of diagnostic tools for detecting cardiac arrhythmias: systematic literature search. *Neth Heart J*. Nov 2010;18(11):543-551. PMID 21113379
 11. Turakhia MP, Hoang DD, Zimetbaum P, et al. Diagnostic utility of a novel leadless arrhythmia monitoring device. *Am J Cardiol*. Aug 15 2013;112(4):520-524. PMID 23672988
 12. Barrett PM, Komatireddy R, Haaser S, et al. Comparison of 24-hour Holter monitoring with 14-day novel adhesive patch electrocardiographic monitoring. *Am J Med*. Jan 2014;127(1):95 e11-97. PMID 24384108
 13. Solomon MD, Yang J, Sung SH, et al. Incidence and timing of potentially high-risk arrhythmias detected through long term continuous ambulatory electrocardiographic monitoring. *BMC Cardiovasc Disord*. Feb 17 2016;16(1):35. PMID 26883019
 14. Bolourchi M, Batra AS. Diagnostic yield of patch ambulatory electrocardiogram monitoring in children (from a national registry). *Am J Cardiol*. Mar 1 2015;115(5):630-634. PMID 25591894
 15. Health Quality Ontario. Long-Term Continuous Ambulatory ECG Monitors and External Cardiac Loop Recorders for Cardiac Arrhythmia: A Health Technology Assessment. *Ont Health Technol Assess Ser*. Feb 2017;17(1):1-56. PMID 28194254
 16. Eisenberg EE, Carlson SK, Doshi RH, et al. Chronic ambulatory monitoring: results of a large single-center experience. *J Innovations Cardiac Rhythm Manage*. Nov 2014;5:1818-1823.
 17. Schreiber D, Sattar A, Drigalla D, et al. Ambulatory cardiac monitoring for discharged emergency department patients with possible cardiac arrhythmias. *West J Emerg Med*. Mar 2014;15(2):194-198. PMID 24672611
 18. Dagues N, Kottkamp H, Piorkowski C, et al. Influence of the duration of Holter monitoring on the detection of arrhythmia recurrences after catheter ablation of atrial fibrillation: implications for patient follow-up. *Int J Cardiol*. Mar 18 2010;139(3):305-306. PMID 18990460
 19. Pokushalov E, Romanov A, Corbucci G, et al. Ablation of paroxysmal and persistent atrial fibrillation: 1-year follow-up through continuous subcutaneous monitoring. *J Cardiovasc Electrophysiol*. Apr 2011;22(4):369-375. PMID 20958836

20. Chao TF, Lin YJ, Tsao HM, et al. CHADS(2) and CHA(2)DS(2)-VASc scores in the prediction of clinical outcomes in patients with atrial fibrillation after catheter ablation. *J Am Coll Cardiol*. Nov 29 2011;58(23):2380-2385. PMID 22115643
21. Kapa S, Epstein AE, Callans DJ, et al. Assessing arrhythmia burden after catheter ablation of atrial fibrillation using an implantable loop recorder: the ABACUS study. *J Cardiovasc Electrophysiol*. Aug 2013;24(8):875-881. PMID 23577826
22. Verma A, Champagne J, Sapp J, et al. Discerning the incidence of symptomatic and asymptomatic episodes of atrial fibrillation before and after catheter ablation (DISCERN AF): a prospective, multicenter study. *JAMA Intern Med*. Jan 28 2013;173(2):149-156. PMID 23266597
23. Themistoclakis S, Corrado A, Marchlinski FE, et al. The risk of thromboembolism and need for oral anticoagulation after successful atrial fibrillation ablation. *J Am Coll Cardiol*. Feb 23 2010;55(8):735-743. PMID 20170810
24. Gumbinger C, Krumsdorf U, Veltkamp R, et al. Continuous monitoring versus HOLTER ECG for detection of atrial fibrillation in patients with stroke. *Eur J Neurol*. Feb 2012;19(2):253-257. PMID 21895885
25. Lazzaro MA, Krishnan K, Prabhakaran S. Detection of atrial fibrillation with concurrent holter monitoring and continuous cardiac telemetry following ischemic stroke and transient ischemic attack. *J Stroke Cerebrovasc Dis*. Feb 2012;21(2):89-93. PMID 20656504
26. Cotter PE, Martin PJ, Ring L, et al. Incidence of atrial fibrillation detected by implantable loop recorders in unexplained stroke. *Neurology*. Apr 23 2013;80(17):1546-1550. PMID 23535493
27. Miller DJ, Khan MA, Schultz LR, et al. Outpatient cardiac telemetry detects a high rate of atrial fibrillation in cryptogenic stroke. *J Neurol Sci*. Jan 15 2013;324(1-2):57-61. PMID 23102659
28. Sposato LA, Cipriano LE, Saposnik G, et al. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol*. Apr 2015;14(4):377-387. PMID 25748102
29. Kishore A, Vail A, Majid A, et al. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis. *Stroke*. Feb 2014;45(2):520-526. PMID 24385275
30. Kamel H, Navi BB, Eljovich L, et al. Pilot randomized trial of outpatient cardiac monitoring after cryptogenic stroke. *Stroke*. Feb 2013;44(2):528-530. PMID 23192756
31. Higgins P, MacFarlane PW, Dawson J, et al. Noninvasive cardiac event monitoring to detect atrial fibrillation after ischemic stroke: a randomized, controlled trial. *Stroke*. Sep 2013;44(9):2525-2531. PMID 23899913
32. Sinha AM, Diener HC, Morillo CA, et al. Cryptogenic Stroke and underlying Atrial Fibrillation (CRYSTAL AF): design and rationale. *Am Heart J*. Jul 2010;160(1):36-41 e31. PMID 20598970
33. Sanna T, Diener HC, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med*. Jun 26 2014;370(26):2478-2486. PMID 24963567
34. Brachmann J, Morillo CA, Sanna T, et al. Uncovering atrial fibrillation beyond short-term monitoring in cryptogenic stroke patients: three-year results from the Cryptogenic Stroke and Underlying Atrial Fibrillation Trial. *Circ Arrhythm Electrophysiol*. Jan 2016;9(1):e003333. PMID 26763225
35. Gladstone DJ, Spring M, Dorian P, et al. Atrial fibrillation in patients with cryptogenic stroke. *N Engl J Med*. Jun 26 2014;370(26):2467-2477. PMID 24963566

36. Ritter MA, Kochhauser S, Duning T, et al. Occult atrial fibrillation in cryptogenic stroke: detection by 7-day electrocardiogram versus implantable cardiac monitors. *Stroke*. May 2013;44(5):1449-1452. PMID 23449264
37. Etgen T, Hochreiter M, Mundel M, et al. Insertable cardiac event recorder in detection of atrial fibrillation after cryptogenic stroke: an audit report. *Stroke*. Jul 2013;44(7):2007-2009. PMID 23674523
38. Tung CE, Su D, Turakhia MP, et al. Diagnostic yield of extended cardiac patch monitoring in patients with stroke or TIA. *Front Neurol*. Jan 2014;5:266. PMID 25628595
39. Rosenberg MA, Samuel M, Thosani A, et al. Use of a noninvasive continuous monitoring device in the management of atrial fibrillation: a pilot study. *Pacing Clin Electrophysiol*. Mar 2013;36(3):328-333. PMID 23240827
40. Savelieva I, Camm AJ. Clinical relevance of silent atrial fibrillation: prevalence, prognosis, quality of life, and management. *J Interv Card Electrophysiol*. Jun 2000;4(2):369-382. PMID 10936003
41. Israel CW, Gronefeld G, Ehrlich JR, et al. Long-term risk of recurrent atrial fibrillation as documented by an implantable monitoring device: implications for optimal patient care. *J Am Coll Cardiol*. Jan 07 2004;43(1):47-52. PMID 14715182
42. Page RL, Wilkinson WE, Clair WK, et al. Asymptomatic arrhythmias in patients with symptomatic paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia. *Circulation*. Jan 1994;89(1):224-227. PMID 8281651
43. Hart RG, Pearce LA, Rothbart RM, et al. Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. *Stroke Prevention in Atrial Fibrillation Investigators*. *J Am Coll Cardiol*. Jan 2000;35(1):183-187. PMID 10636278
44. Hohnloser SH, Pajitnev D, Pogue J, et al. Incidence of stroke in paroxysmal versus sustained atrial fibrillation in patients taking oral anticoagulation or combined antiplatelet therapy: an ACTIVE W Substudy. *J Am Coll Cardiol*. Nov 27 2007;50(22):2156-2161. PMID 18036454
45. Ganesan AN, Chew DP, Hartshorne T, et al. The impact of atrial fibrillation type on the risk of thromboembolism, mortality, and bleeding: a systematic review and meta-analysis. *Eur Heart J*. May 21 2016;37(20):1591-1602. PMID 26888184
46. Fitzmaurice DA, Hobbs FD, Jowett S, et al. Screening versus routine practice in detection of atrial fibrillation in patients aged 65 or over: cluster randomised controlled trial. *BMJ*. Aug 25 2007;335(7616):383. PMID 17673732
47. Halcox JPJ, Wareham K, Cardew A, et al. Assessment of Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation: The REHEARSE-AF Study. *Circulation*. Nov 7 2017;136(19):1784-1794. PMID 28851729
48. Turakhia MP, Ullal AJ, Hoang DD, et al. Feasibility of extended ambulatory electrocardiogram monitoring to identify silent atrial fibrillation in high-risk patients: the Screening Study for Undiagnosed Atrial Fibrillation (STUDY-AF). *Clin Cardiol*. May 2015;38(5):285-292. PMID 25873476
49. Narasimha D, Hanna N, Beck H, et al. Validation of a smartphone-based event recorder for arrhythmia detection. *Pacing Clin Electrophysiol*. Mar 1 2018. PMID 29493801
50. Solbiati M, Casazza G, Dipaola F, et al. The diagnostic yield of implantable loop recorders in unexplained syncope: A systematic review and meta-analysis. *Int J Cardiol*. Mar 15 2017;231:170-176. PMID 28052814

51. Burkowitz J, Merzenich C, Grassme K, et al. Insertable cardiac monitors in the diagnosis of syncope and the detection of atrial fibrillation: A systematic review and meta-analysis. *Eur J Prev Cardiol.* Aug 2016;23(12):1261-1272. PMID 26864396
52. Da Costa A, Defaye P, Romeyer-Bouchard C, et al. Clinical impact of the implantable loop recorder in patients with isolated syncope, bundle branch block and negative workup: a randomized multicentre prospective study. *Arch Cardiovasc Dis.* Mar 2013;106(3):146-154. PMID 23582676
53. Farwell DJ, Freemantle N, Sulke AN. Use of implantable loop recorders in the diagnosis and management of syncope. *Eur Heart J.* Jul 2004;25(14):1257-1263. PMID 15246645
54. Krahn AD, Klein GJ, Yee R, et al. Randomized assessment of syncope trial: conventional diagnostic testing versus a prolonged monitoring strategy. *Circulation.* Jul 3 2001;104(1):46-51. PMID 11435336
55. Podoleanu C, DaCosta A, Defaye P, et al. Early use of an implantable loop recorder in syncope evaluation: a randomized study in the context of the French Healthcare System (FRESH study). *Arch Cardiovasc Dis.* Oct 2014;107(10):546-552. PMID 25241220
56. Giada F, Gulizia M, Francese M, et al. Recurrent unexplained palpitations (RUP) study comparison of implantable loop recorder versus conventional diagnostic strategy. *J Am Coll Cardiol.* May 15 2007;49(19):1951-1956. PMID 17498580
57. Edvardsson N, Garutti C, Rieger G, et al. Unexplained syncope: implications of age and gender on patient characteristics and evaluation, the diagnostic yield of an implantable loop recorder, and the subsequent treatment. *Clin Cardiol.* Oct 2014;37(10):618-625. PMID 24890550
58. Bhangu J, McMahon CG, Hall P, et al. Long-term cardiac monitoring in older adults with unexplained falls and syncope. *Heart.* May 1 2016;102(9):681-686. PMID 26822427
59. Afzal MR, Gunda S, Waheed S, et al. Role of outpatient cardiac rhythm monitoring in cryptogenic stroke: a systematic review and meta-analysis. *Pacing Clin Electrophysiol.* Oct 2015;38(10):1236-1245. PMID 26172621
60. Ciconte G, Saviano M, Giannelli L, et al. Atrial fibrillation detection using a novel three-vector cardiac implantable monitor: the atrial fibrillation detect study. *Europace.* Jul 1 2017;19(7):1101-1108. PMID 27702865
61. Nolker G, Mayer J, Boldt LH, et al. Performance of an Implantable Cardiac Monitor to Detect Atrial Fibrillation: Results of the DETECT AF Study. *J Cardiovasc Electrophysiol.* Dec 2016;27(12):1403-1410. PMID 27565119
62. Sanders P, Purerfellner H, Pokushalov E, et al. Performance of a new atrial fibrillation detection algorithm in a miniaturized insertable cardiac monitor: Results from the Reveal LINQ Usability Study. *Heart Rhythm.* Jul 2016;13(7):1425-1430. PMID 26961298
63. Ziegler PD, Rogers JD, Ferreira SW, et al. Real-world experience with insertable cardiac monitors to find atrial fibrillation in cryptogenic stroke. *Cerebrovasc Dis.* 2015;40(3-4):175-181. PMID 26314298
64. Hindricks G, Pokushalov E, Urban L, et al. Performance of a new leadless implantable cardiac monitor in detecting and quantifying atrial fibrillation: Results of the XPECT trial. *Circ Arrhythm Electrophysiol.* Apr 2010;3(2):141-147. PMID 20160169
65. Hanke T, Charitos EI, Stierle U, et al. Twenty-four-hour holter monitor follow-up does not provide accurate heart rhythm status after surgical atrial fibrillation ablation therapy: up to 12

- months experience with a novel permanently implantable heart rhythm monitor device. *Circulation*. Sep 15 2009;120(11 Suppl):S177-184. PMID 19752365
66. Mittal S, Sanders P, Pokushalov E, et al. Safety profile of a miniaturized insertable cardiac monitor: results from two prospective trials. *Pacing Clin Electrophysiol*. Dec 2015;38(12):1464-1469. PMID 26412309
 67. Rothman SA, Laughlin JC, Seltzer J, et al. The diagnosis of cardiac arrhythmias: a prospective multi-center randomized study comparing mobile cardiac outpatient telemetry versus standard loop event monitoring. *J Cardiovasc Electrophysiol*. Mar 2007;18(3):241-247. PMID 17318994
 68. Derkac WM, Finkelmeier JR, Horgan DJ, et al. Diagnostic yield of asymptomatic arrhythmias detected by mobile cardiac outpatient telemetry and autotrigger looping event cardiac monitors. *J Cardiovasc Electrophysiol*. Dec 2017;28(12):1475-1478. PMID 28940881
 69. Kadish AH, Reiffel JA, Clauser J, et al. Frequency of serious arrhythmias detected with ambulatory cardiac telemetry. *Am J Cardiol*. May 1 2010;105(9):1313-1316. PMID 20403485
 70. Joshi AK, Kowey PR, Prystowsky EN, et al. First experience with a Mobile Cardiac Outpatient Telemetry (MCOT) system for the diagnosis and management of cardiac arrhythmia. *Am J Cardiol*. Apr 1 2005;95(7):878-881. PMID 15781022
 71. Olson JA, Fouts AM, Padanilam BJ, et al. Utility of mobile cardiac outpatient telemetry for the diagnosis of palpitations, presyncope, syncope, and the assessment of therapy efficacy. *J Cardiovasc Electrophysiol*. May 2007;18(5):473-477. PMID 17343724
 72. Saarel EV, Doratotaj S, Sterba R. Initial experience with novel mobile cardiac outpatient telemetry for children and adolescents with suspected arrhythmia. *Congenit Heart Dis*. Jan-Feb 2008;3(1):33-38. PMID 18373747
 73. Tayal AH, Tian M, Kelly KM, et al. Atrial fibrillation detected by mobile cardiac outpatient telemetry in cryptogenic TIA or stroke. *Neurology*. Nov 18 2008;71(21):1696-1701. PMID 18815386
 74. Favilla CG, Ingala E, Jara J, et al. Predictors of finding occult atrial fibrillation after cryptogenic stroke. *Stroke*. May 2015;46(5):1210-1215. PMID 25851771
 75. Kalani R, Bernstein R, Passman R, et al. Low yield of mobile cardiac outpatient telemetry after cryptogenic stroke in patients with extensive cardiac imaging. *J Stroke Cerebrovasc Dis*. Sep 2015;24(9):2069-2073. PMID 26139455
 76. Steinberg JS, Varma N, Cygankiewicz I, et al. 2017 ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry. *Heart Rhythm*. Jul 2017;14(7):e55-e96. PMID 28495301
 77. Shen WK, Sheldon RS, Benditt DG, et al. 2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. Aug 1 2017;70(5):620-663. PMID 28286222
 78. Crawford MH, Bernstein SJ, Deedwania PC, et al. ACC/AHA Guidelines for Ambulatory Electrocardiography. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the Guidelines for Ambulatory Electrocardiography). Developed in collaboration with the North American Society for Pacing and Electrophysiology. *J Am Coll Cardiol*. Sep 1999;34(3):912-948. PMID 10483977
 79. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection,

- procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *J Interv Card Electrophysiol*. Mar 2012;33(2):171-257. PMID 22382715
80. Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary. *J Arrhythm*. Oct 2017;33(5):369-409. PMID 29021841
81. Task Force members, Brignole M, Vardas P, et al. Indications for the use of diagnostic implantable and external ECG loop recorders. *Europace*. May 2009;11(5):671-687. PMID 19401342
82. Culebras A, Messe SR, Chaturvedi S, et al. Summary of evidence-based guideline update: prevention of stroke in nonvalvular atrial fibrillation: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. Feb 25 2014;82(8):716-724. PMID 24566225
83. Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for Electrocardiographic Services (20.15). 2004; <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?MCDId=16&ExpandComments=n&McdName=Thomson+Micromedex+DrugDex+%C2%AE+Compendium+Revision+Request+-+CAG-00391&NCDId=179>. Accessed March 19, 2018.
84. BCBSA. Medical Policy Reference Manual. Ambulatory Event Monitors and Mobile Outpatient Cardiac Telemetry. #2.02.08. Reviewed May 2018.