Technology Assessment

Technology Assessment Program

Remote Cardiac Monitoring

Agency for Healthcare Research and Quality
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Remote Cardiac Monitoring

A Systematic Review

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EXECUTIVE SUMMARY

The Centers for Medicare & Medicaid Services (CMS) requested that the Agency for Healthcare Research and Quality (AHRQ) commission an evidence report to evaluate remote cardiac monitoring devices. Accordingly, on November 9, 2006, AHRQ, in consultation with CMS and ECRI Institute, issued a Statement of Work (SOW) contracting ECRI Institute to prepare an evidence report on this topic.

Scope and Background

Remote cardiac monitoring technologies allow home electrocardiographic (ECG) monitoring of patients with suspected cardiac arrhythmias or at risk for developing arrhythmias. Two major categories of remote cardiac monitoring devices are evaluated in this report. The first category consists of patient- or event-activated devices, which include externally-worn pre-symptom memory loop recorders (attended and unattended), implantable/insertable pre-symptom memory loop recorders (attended and unattended), and post-symptom patient-activated recorders. The second category comprises real-time continuous attended cardiac monitoring systems. These devices are described in detail under Evidence Synthesis, Key Question 1.

Continuous unattended cardiac monitoring (e.g., Holter monitoring) is beyond the scope of this report. Pre-hospital (in ambulance) monitoring and transmission, as well as monitoring solely for the purpose of detecting device failure, are also beyond the scope of this report.

The patient population of interest in this report consists of patients with suspected cardiac arrhythmias manifesting through symptoms such as syncope (transient loss of consciousness), presyncope, dizziness, palpitations, and other symptoms that could be attributed to arrhythmia. Patients with life-threatening arrhythmias would not be considered candidates for these technologies. Patients with primary non-cardiac diagnoses (e.g., epilepsy) are beyond the scope of this report.

Key Questions

In commissioning this report, AHRQ, in consultation with CMS and ECRI Institute, developed seven Key Questions to be addressed. These seven Key Questions are presented below.

Key Question 1: **What types of devices/techniques are currently available to remotely assess cardiac rhythm abnormalities in ambulatory patients? These categories will include:**

- ***a.*** **Patient- or event-activated devices, such as pre-symptom memory loop recorders (attended and unattended), implantable (or insertable) pre-symptom memory loop recorders (attended and unattended), and post-symptom recorders with transtelephonic transmission of ECG data (unattended)**
- ***b.*** **Real-time continuous attended cardiac monitoring**

Key Question 2: **How is patient eligibility for remote cardiac monitoring (1.a and b) determined?**

Key Question 3: **Is management changed based on information obtained from remote cardiac monitoring using any of the identified categories of devices and do these changes lead to improvements in the following outcomes in ambulatory patients (or a subgroup of ambulatory patients)?**

- ***a.*** **Palpitations**
- ***b.*** **Syncopal episodes**
- ***c.*** **Transient ischemic attacks (TIAs) and non-fatal stroke**
- ***d.*** **Dizziness and other pre-syncopal symptoms**
- ***e.*** **Dyspnea or heart failure**
- ***f.*** **Angina or myocardial infarction (MI)**
- ***g.*** **Mortality**
- ***h.*** **Quality of life**

Key Question 4: **Of the patient outcomes for which improvements have been demonstrated, do any categories of devices (as listed under Question 1) lead to greater improvement in these outcomes in ambulatory patients (or a subgroup of ambulatory patients) compared to any of the other categories of devices?**

Key Question 5: **Of the patient outcomes for which improvements have been demonstrated, do any devices within a category lead to greater improvement in these outcomes in ambulatory patients (or a subgroup of ambulatory patients) compared to any of the other devices within the same category?**

Key Question 6: **What accreditation standards exist for training and continuing education for the interpretation of data from remote cardiac monitoring?**

Key Question 7: **What standards exist to guide how data gathered from remote cardiac monitors should be incorporated into a patient's continuum of care? In practice (i.e., as reported in the published literature, "gray literature," etc.), what are the characteristics of the patient care infrastructure using remote cardiac monitoring (e.g., use of either attending technicians or attending physicians) and how are the data gathered from remote cardiac monitoring used to inform patients' continuum of care?**

Data Sources

We searched 16 external and internal databases, including PubMed and EMBASE, for clinical trials on the use of real-time remote attended continuous cardiac monitoring. In addition, we routinely reviewed more than 1,600 journals and supplements maintained in ECRI's collections to determine if they contained relevant information. We also examined the bibliographies/reference lists from peer-reviewed and gray literature. For Key Questions 3, 4, and 5, we only considered published, peer-reviewed literature. For Key Questions 1, 2, 6, and 7, we examined other sources (including gray literature) to identify relevant information.

Evidence Bases

Key Questions 1, 2, 6, and 7 did not involve an evaluation of clinical evidence; therefore, we do not include them in our discussion of evidence bases.

Our searches identified 429 articles that potentially addressed Key Questions 3 through 5. Of these 429 articles, we retrieved 97. Twenty included articles addressed Key Question 3 (although only 17 were used in the analysis), three included studies addressed Key Question 4, and no included articles addressed Key Question 5.

Main Findings and Conclusions

Key Question 1: What types of devices/techniques are currently available to remotely assess cardiac rhythm abnormalities in ambulatory patients?

Several devices are currently used to remotely assess cardiac rhythm abnormalities in ambulatory patients. These devices can be categorized according to whether they monitor cardiac rhythm intermittently or continuously, and whether they are worn externally or implanted.

Patient/event-activated intermittent recorders (pre-symptom continuous loop and post-symptom recorders) comprise the largest category. Devices in this category monitor ECG rhythms but do not continuously record data. Data can be transmitted by phone to a doctor's office, clinic, or hospital (some devices also can upload data to a PC). Intermittent recorders can be further subcategorized as externally-worn or implantable, whether they have memory loop-recording capability (see main text for further explanation), and whether they offer both automatic and patient-triggered transmission of monitoring data or only patient-activated transmissions. Remote monitoring centers can provide attended monitoring services (using technicians or other medical personnel) for these devices; Independent Diagnostic Testing Facilities (IDTF) are an important provider of these services.

The standard external loop recorder (ELR) records several minutes of activity at a time and then starts over, a process referred to as memory loop recording. The patient

activates this device to record when a symptom occurs and then data from the device is typically transmitted to a monitoring center for immediate review. This process is repeated whenever symptoms occur over a period of 20 to 30 days (which is the typical amount of time the device is worn by the patient). Since the data that are recorded by the device are typically associated with a symptom, a physician can also determine whether that symptom is a result of a cardiac arrhythmia. When a patient experiences the symptoms of an event, he or she holds the device next to his or her chest and activates the device to begin recording. However, due to the need for the patient to signal an event, the standard cardiac event monitor typically only captures events associated with a patient's symptoms and not those events that are asymptomatic.

The auto-trigger ELR also memory loop records, capturing several minutes of heart activity at a time before starting over. In addition, however, the auto-trigger ELR uses systems to automatically detect events that may not be associated with a patient experiencing symptoms. Unlike a standard ELR, an auto-trigger ELR does not rely on the patient's ability to activate it and, as a result, is able to capture asymptomatic events in addition to symptomatic ones. However, the auto-trigger device still relies on the patient to call in and transmit the event by reaching the physician or a technician at a physician's office or a monitoring center and holding the cardiac event monitor up to a telephone to transmit the event data.

Implantable/insertable loop recorders (ILRs) perform the same function as ELRs, except that they are implanted subcutaneously in the left or right chest region. The main difference between ILRs and ELRs is that ILRs can be used for a much longer time period (current models offer 14-20 months of longevity) before being surgically removed. Currently, the only commercially-available ILRs are the Reveal® Plus (Medtronic) and the Sleuth™ (Transoma Medical), both of which can be programmed for automatic activation or patient activation. Unlike Reveal® Plus, which cannot transmit ECG data from home, Sleuth is a wireless system which can transmit ECG data to a remote monitoring center.

Post-symptom event monitors are hand-held devices that have no chest electrodes. These monitors lack the memory loop of pre-symptom recorders and can therefore only record the rhythm that occurs after being triggered by the patient. They generally do not have automatic activation upon occurrence of asymptomatic arrhythmias.

Real-time continuous attended remote cardiac monitoring systems automatically record and transmit arrhythmic event data from ambulatory patients to personnel monitoring, or attending the monitor, at a clinic or hospital. Four such systems are currently commercially marketed: The CardioNet system (CardioNet, Inc), the HEARTLink II system (Cardiac Telecom Corp), the VST^{TM} (Vital Signs Transmitter, Biowatch Medical), and the CG-6108 continuous ECG monitor, also known as the Lifestar ambulatory cardiac telemetry (ACT) system (Card Guard Scientific Survival Ltd.).(1-3) These systems allow automatic wireless transmission of abnormal ECG waveforms at the time of event occurrence from the patient's home to an attended monitoring center. In addition, the CardioNet system has a built-in cellular telephone that automatically transmits arrhythmic signals to the monitoring center when the patient is away from home.

Key Question 2: **How is patient eligibility for remote cardiac monitoring (1.a and b) determined?**

Patient eligibility for remote cardiac monitoring is determined primarily by considering patient characteristics, mostly sporadic symptoms (such as syncope, palpitations, or dizziness) suspected to be caused by arrhythmias.

Three recent guidelines propose separate indications for continuous Holter monitoring and intermittent event monitoring (with external or implanted devices). A 2006 American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) guideline on management of patients with ventricular arrhythmias states that continuous 24-48 hour Holter recordings are deemed appropriate when arrhythmias are known or suspected to occur at least once a day. Because intermittent event monitors can record over longer time periods, they are considered more appropriate when sporadic episodes produce symptoms of syncope, dizziness, or

palpitations. The document does not provide clear indications for when external versus implantable event monitors should be used, although it suggests implantable recorders are useful in patients with sporadic symptoms suspected to be arrhythmia-related in whom a symptom-rhythm correlation has not been established by conventional diagnostic techniques. This guideline makes no mention of real-time continuous attended monitoring systems.

A 2004 British Columbia Health Services guideline on ambulatory electrocardiographic (ECG) monitoring similarly suggests that patients with daily or almost daily symptoms or those with syncope without warning may be evaluated with a 24-hour Holter monitor. Patients with less frequent symptoms may be better evaluated using a patient-activated event recorder. (Automatic recorders are not mentioned, nor are real-time continuous attended monitoring systems).

A 2004 European Society of Cardiology guideline on management of syncope also suggests Holter monitoring as the initial strategy in patients with clinical or ECG features of arrhythmic syncope and very frequent syncopes or presyncopes (Class I indication). Unlike other guidelines, this one states that an ILR is indicated if the mechanism of syncope remains unclear after Holter monitoring in patients with very frequent episodes of syncope (Class I indication). In patients with features of arrhythmic syncope occurring at intervals ≤4 weeks, an ELR may be used (Class II indication). An ILR may be indicated to assess the contribution of bradycardia before implanting a pacemaker in patients with suspected or certain neurally-mediated forms of syncope with frequent or traumatic syncopal episodes (Class II indication). An ILR may also be indicated in the initial phase of the work-up instead of conventional investigations in patients with preserved cardiac function who have features suggesting an arrhythmic syncope (Class II indication).

A 2006 American Heart Association/American College of Cardiology Scientific Statement on the evaluation of syncope suggests that ambulatory electrocardiography (AECG) is appropriate in patients with syncope who have had a “normal” evaluation (no underlying heart disease detected) and the diagnosis remains uncertain. The document

states that a Holter monitor is appropriate for episodes that occur at least every day, and event monitoring is ideal for episodes that occur at least once a month. An ILR is considered the most likely technology to identify the mechanism of syncope in patients with unexplained syncope.

A clinical competence statement published by the American College of Cardiology and the American Heart Association suggests that the frequency of symptoms should dictate the type of recording device used. This statement also suggests that for patients with infrequent symptoms, intermittent event recorders may be more cost-effective than continuous Holter monitors.

Continuous recording devices are indicated for use in patients with frequent symptoms (at least once a day) that may be arrhythmia-related, for patients with syncope or near syncope, and for patients with recurrent unexplained palpitations. Continuous monitoring is also indicated for patients receiving anti-arrhythmic therapy to assess drug response, to monitor the rate of atrial fibrillation, and to exclude proarrythmia.

For patients with pacemakers or implantable cardioverter defibrillators (ICDs), continuous monitoring is indicated to assess the device for myopotential inhibition and pacemaker-mediated tachycardia; to help optimize physiologic programming; to evaluate whether a pacemaker or ICD stopped functioning; and to assess concomitant drug therapy.

Continuous monitoring may also be useful in assessing silent ischemia and monitoring anti-ischemia therapy.

Key Question 3: **Is management changed based on information obtained from remote cardiac monitoring using any of the identified categories of devices and do these changes lead to improvements in the following outcomes in ambulatory patients (or a subgroup of ambulatory patients)?**

a. **Palpitations**

b. **Syncopal episodes**

c. **TIAs and non-fatal stroke**

d. **Dizziness and other pre-syncopal symptoms**

e. **Dyspnea and heart failure**

f. **Angina and MI**

g. **Mortality**

h. **Quality of life**

Overall Conclusions: Patients with unexplained syncope are more likely to undergo a change in disease management when using ILR monitoring or real-time continuous attended monitoring than when using conventional assessment (i.e., Holter monitoring and/or tilt table testing). Patients with severe palpitations occurring less than once per 24 hours are also more likely to undergo a change in disease management when using real-time continuous attended monitoring. The strength of evidence is moderate for ILR (based on 13 studies, overall quality moderate), and weak for real-time continuous monitoring (based on one high-quality multicenter trial). Due to small numbers of studies identified and numerous quality flaws, the evidence was insufficient to evaluate the effect of other remote monitoring devices (ELRs and post-event recorders) on change in disease management. For the same reasons, the evidence is also insufficient to determine whether any class of remote cardiac monitoring devices leads to better clinical outcomes than conventional monitoring.

ILR – Evidence Summary

Changes in Disease Management: One randomized controlled trial (RCT) and 12 uncontrolled case series with a total of 758 patients reported information on changes in disease management after ILR implantation in patients with suspected cardiac arrhythmias based on symptoms of syncope or presyncope (in 11 of 13 studies all patients had syncope). All of these studies evaluated patients with a potential arrhythmia who had remained undiagnosed after Holter monitoring and/or tilt table testing. Our synthesis of these studies indicated that a significantly larger number of patients with unexplained syncope undergo changes in disease management with ILR monitoring than with conventional arrhythmia assessment. (Change in management was dependent upon obtaining a diagnosis during monitoring.) Multiple sensitivity analyses supported the robustness of this conclusion. The strength of evidence

supporting this conclusion is moderate (see Table 2 in main text for a description of strength ratings).

Syncopal Episodes: Four studies (one RCT, two case series, and a single arm from a controlled trial) with a total of 369 patients reported syncopal episodes after ILR implantation. These studies varied in quality (the RCT high, two moderate, and one low). The data were not combined because reduction in syncope was reported using different methods of measurement (% syncope recurrence, mean syncope rates before and after ILR, time to second syncope, etc.), and the findings were inconsistent for the different measurements (some were statistically significant, others were not). Also, one non-randomized study made a comparison among patients who underwent ILR monitoring but did not all receive ILR-based treatment, while the RCT compared syncope outcomes among patients who did and did not undergo ILR monitoring. The only high-quality study with a parallel control group (of patients who underwent conventional assessment) found a statistically significant increase in the time to second syncope associated with ILR monitoring but no statistically significant decrease in the recurrence rate. However, the providers were not blinded and the between-group difference in time to recurrence ($p = 0.04$) was not large enough to allow a conclusion based on one single-center study. These findings differed somewhat from the low-quality case series with a subsequent comparison, which found a statistically significant reduction in syncope recurrence associated with ILR monitoring. However, this study was not randomized or blinded and showed evidence of selection bias (patients with asystole were predominantly selected for the specific therapy group), and the comparison differs somewhat from the comparison in the RCT (which was based on syncope recurrence among any patients in the two arms, not just among diagnosed patients). Because of these differences, and because the two other studies lacked essential comparative data, the evidence is insufficient to reach a conclusion for this outcome.

Mortality: Three studies (one RCT, two case series) with a total of 389 patients with at least one year of followup reported mortality after ILR implantation. The RCT showed no statistically significant difference between groups, but the 95% confidence interval

(CI) was too wide to exclude the possibility of a substantial mortality difference. Also, the case series data did not distinguish between deaths among diagnosed patients versus undiagnosed patients, so no analysis could be performed. Thus, the evidence is insufficient to determine whether differences in mortality rates exist between patients receiving ILR and patients receiving only conventional assessment.

Quality of Life: One RCT reported quality-of-life data, measured using the SF-12 questionnaire and a visual analogue scale (VAS) for general well-being. However, because this is a single-center study without a demonstrably large difference in effect between the ILR and control groups, and the different quality-of-life instruments showed inconsistent findings, the evidence is insufficient to allow a conclusion regarding quality of life.

Other outcomes: One study reported data on palpitations that could not be interpreted due to lack of adequate comparative data.

ELRs – Evidence Summary

Change in Management: Four studies with 318 patients reported change-in-management data in patients monitored by ELRs. Indications for monitoring in one study were exclusively unexplained syncope; indications in another study included syncope, presyncope, or palpitations; indications in a third study were exclusively palpitations; and indications in the fourth study were prior acute stroke or transient ischemic attack (TIA). Because of this clinical heterogeneity in patient characteristics, the data from these studies were not combined. Because the studies were of low-to-moderate quality and no data were available for estimating a control group change-in-management rate, the evidence was insufficient to allow any conclusion about the effect of ELRs on patient management.

Syncopal Episodes: One RCT comparing ELR to ILR reported resolution of syncope among diagnosed patients; for this question, we considered only the patients who underwent ELR monitoring (6/6 diagnosed patients had resolution of syncope). Management was changed for only four of these patients following diagnosis, and the authors did not report the number of undiagnosed patients who had resolution of

syncope. Thus, the evidence is insufficient to determine whether ELR is associated with a reduction in syncopal episodes.

Post-event Recorders – Evidence Summary

Change in Management: One randomized crossover study with 45 patients reported change-in-management data in patients monitored by post-event recorders. This study included only patients with palpitations. Although eight of 45 patients underwent a change in management after post-event monitoring and none changed management after conventional assessment with a Holter monitor, the conventional assessment period was much shorter (two days) than the post-event monitoring period (three months). Thus, this trial is similar to case series of patients who had non-diagnostic Holter monitoring prior to a longer-duration remote monitoring technology. Since this was a single, small, moderate-quality study, the evidence was insufficient to allow any conclusions about the utility of post-event recorders.

Other outcomes: One study reported data on palpitations that could not be interpreted due to lack of adequate comparative data.

Real-Time Continuous Attended Systems – Evidence Summary

Change in Management: One multicenter RCT with a total of 266 patients compared monitoring with a real-time continuous attended system to monitoring with ELRs; for the purposes of this question, the ELR detection rate was assumed to be not lower than the success rate of conventional assessment, as the patients had undergone prior conventional assessment without being diagnosed. Indications for monitoring included symptoms of syncope, presyncope, or severe palpitations occurring less than once per 24 hours. This was a high-quality multicenter trial that found that a substantially larger number of patients had clinically significant arrhythmias (requiring management change) detected in the real-time group (41%, 55/134 patients) compared to the ELR group (14%, 19/132 patients), a roughly three-fold difference that was statistically significant. Thus, the evidence is sufficient to conclude that real-time monitoring leads to a change in disease management in significantly more patients than does conventional

assessment. Although the quality of this multicenter study is high, the strength of evidence supporting this conclusion is weak because it has not yet been replicated.

Other outcomes: No published studies of any remote cardiac monitoring technology reported data on the following outcomes: dizziness, TIAs and non-fatal stroke, dyspnea or heart failure, and angina or myocardial infarction (MI).

Key Question 4: **Of the patient outcomes for which improvements have been demonstrated, do any categories of devices (as listed under Question 1) lead to greater improvement in these outcomes in ambulatory patients (or a subgroup of ambulatory patients) compared to any of the other categories of devices?**

Three RCTs with 376 patients addressed this question. Two studies with 110 patients compared a prolonged monitoring strategy with ILR to a strategy using ELR plus other tests (tilt table testing and/or electrophysiological testing) for assessment of unexplained syncope (one study) or palpitations (one study). These studies found a statistically significant increase in the proportion of patients who underwent a change in management in the ILR group compared to the ELR group. However, these studies had several limitations, including between-group differences in baseline patient characteristics and lack of blinding of outcome assessors. Furthermore, the two studies each evaluated clinically different patient populations (patients with palpitations vs patients with syncope), which precluded combining the data in a meta-analysis. Because these are small, single-center studies of only moderate quality, the evidence is insufficient to allow a conclusion about the relative benefits of ILRs and ELRs in patients with unexplained syncope or palpitations.

The other study (266 patients) compared real-time continuous attended monitoring with ELR, and found that a substantially larger number of patients had clinically significant arrhythmias (requiring management change) detected in the real-time group (55/134 patients) compared to the ELR group (19/132 patients), a roughly three-fold difference that was statistically significant. Most participating centers used patient-activated ELRs, while two of the centers used ELRs with automatic event activation. This study was a high-quality multicenter study with few limitations. Therefore, the evidence is sufficient

to conclude that real-time continuous attended monitoring leads to change in disease management in significantly more patients than do certain ELRs. Because this is a single multicenter study, the strength of evidence supporting this conclusion is weak. Also, the conclusion may not be applicable to ELRs with automatic event activation, as this model was underrepresented in the RCT (only 16% of patients received this model).

One study comparing ILR monitoring to ELR monitoring evaluated a patient-oriented outcome (reduction in syncope). However, because the comparison was inadequately controlled in this single study, the evidence was insufficient to allow a conclusion for this outcome. No other patient-oriented outcomes were evaluated by any studies in this evidence base.

***Key Question 5*: Of the patient outcomes for which improvements have been demonstrated, do any devices within a category lead to greater improvement in these outcomes in ambulatory patients (or a subgroup of ambulatory patients) compared to any of the other devices within the same category?**

Our searches identified no studies that addressed this question.

***Key Question 6*: What accreditation standards exist for training and continuing education for the interpretation of data from remote cardiac monitoring?**

Standards for training in ambulatory electrocardiography (AECG) generally expect trainees to meet the same competence criteria required for interpretation of classic 12-lead ECG. ACC/AHA recommends supervised interpretation of a minimum of 150 AECGs be considered necessary for minimum competence. To maintain competence, ACC/AHA recommends physicians complete a minimum of 25 interpretations per year and that an expert review their interpretations for quality assurance purposes. A guideline from the Cardiac Society of Australia and New Zealand recommends that at least 100 AECGs spanning the range from abnormal to normal should be read and interpreted by a supervised postgraduate student.

Credentialing criteria in the United States are addressed by a Joint Commission document that states that Contracted Licensed Independent Practitioners (LIPs) who read and interpret data transmitted to a remote site need to be credentialed and privileged at both the distant and originating (facility receiving the telemedicine service) site. If the remote site is a Joint Commission-accredited organization, the prescribing site may use both the credentialing and privileging decisions from the remote site. In cases where the remote site is not Joint Commission-accredited or if the practitioner was hired directly, the originating site is responsible for credentialing and privileging that practitioner as if he/she was at the original site.

Key Question 7: **What standards exist to guide how data gathered from remote cardiac monitors should be incorporated into a patient's continuum of care? In practice (i.e., as reported in the published literature, "gray literature," etc), what are the characteristics of the patient care infrastructure using remote cardiac monitoring (e.g., use of either attending technicians or attending physicians) and how are the data gathered from remote cardiac monitoring used to inform patients' continuum of care?**

Our searches identified no formal standards that addressed this question. However, information regarding the patient care infrastructure for remote cardiac monitoring systems is available from manufacturer Web sites, Food and Drug Administration (FDA) documents and published articles. Information relevant to this question was obtained primarily from manufacturer Web sites and FDA documents; studies that addressed Key Questions 3 and 4 did not provide any additional information on infrastructure that was not reported by these other sources. Important issues in patient care infrastructure include methods of data collection, whether monitoring is attended or unattended, who collects and analyzes the data, what is the patient care protocol, and what information becomes part of the medical record. More of these types of information was available on devices that transmit ECG data to attended monitoring centers (which includes all of the remote continuous attended monitoring devices). Attended monitoring centers are usually staffed by technicians (or occasionally other health professionals) who analyze ECG data and report critical events to a patient's physician. Some centers send daily

reports and/or a final summary report to the physician, and data are generally accessible to the physician at all times. The majority of patient- or event-activated intermittent recorders (looping or post-event) at least have the option of being attended by a fully-staffed monitoring center. Patient care protocols generally are not well described for most devices. However, stored ECG data are usually accessible by physicians during the monitoring period. The information that is incorporated into medical records was not clearly described in source documents for any of these devices, although we assume that, at a minimum, important events and diagnoses are entered into these records.

Overall Summary

This report is a systematic review focused on the downstream utility of a diagnostic technology. At a minimum, such a review needs to evaluate whether diagnosis actually leads to a change in clinical management, and ideally the review should evaluate whether the diagnosis ultimately leads to improved patient-oriented outcomes. Most of the studies in the field are focused on the question “does the technology lead to an appropriate diagnosis,“ and any downstream outcomes are less likely to be reported. Some clinicians assume that a patient’s quality of life will improve simply from receiving a diagnosis, regardless of whether management is changed. However, this assumption remains an assumption in the absence of quality-of-life data obtained from validated instruments. While this report did find evidence that certain remote cardiac monitoring technologies lead to changes in patient management, the available evidence was insufficient to allow conclusions about the impact of remote cardiac monitoring technologies on any patient-oriented outcomes. Future studies that focus on downstream patient-oriented outcomes would be useful for determining the true benefit of these technologies.

SCOPE OF REPORT

The Centers for Medicare & Medicaid Services (CMS) requested that the Agency for Healthcare Research and Quality (AHRQ) commission an evidence report to evaluate remote cardiac monitoring devices. Accordingly, on November 9, 2006, AHRQ, in consultation with CMS and ECRI Institute, issued a Statement of Work (SOW) contracting ECRI Institute to prepare an evidence report on this topic. AHRQ, in consultation with CMS and ECRI institute, developed seven Key Questions to be addressed. These questions are as follows:

1. What types of devices/techniques are currently available to remotely assess cardiac rhythm abnormalities in ambulatory patients?
2. How is patient eligibility for remote cardiac monitoring (1.a and b) determined?
3. Is management changed based on information obtained from remote cardiac monitoring using any of the identified categories of devices and do these changes lead to improvements in the following outcomes in ambulatory patients (or a subgroup of ambulatory patients)?
    a. Palpitations
    b. Syncopal episodes
    c. Transient ischemic attacks (TIAs) and non-fatal stroke
    d. Dizziness and other pre-syncopal symptoms
    e. Dyspnea and heart failure
    f. Angina and myocardial infarction (MI)
    g. Mortality
    h. Quality of life
4. Of the patient outcomes for which improvements have been demonstrated, do any categories of devices (as listed under Question 1) lead to greater improvement in these outcomes in ambulatory patients (or a subgroup of ambulatory patients) compared to any of the other categories of devices?

5. Of the patient outcomes for which improvements have been demonstrated, do any devices within a category lead to greater improvement in these outcomes in ambulatory patients (or a subgroup of ambulatory patients) compared to any of the other devices within the same category?
6. What accreditation standards exist for training and continuing education for the interpretation of data from remote cardiac monitoring?
7. What standards exist to guide how data gathered from remote cardiac monitors should be incorporated into a patient's continuum of care? In practice (i.e., as reported in the published literature, "gray literature," etc.), what are the characteristics of the patient care infrastructure using remote cardiac monitoring (e.g., use of either attending technicians or attending physicians) and how are the data gathered from remote cardiac monitoring used to inform patients' continuum of care?

Two major categories of remote cardiac monitoring devices are evaluated in this report. The first category consists of patient- or event-activated devices, which include externally-worn pre-symptom memory loop recorders (attended and unattended), implantable/insertable pre-symptom memory loop recorders (attended and unattended), and post-symptom patient-activated recorders. The second category comprises real-time continuous attended cardiac monitoring systems. These devices are described in detail under Evidence Synthesis, Key Question 1.

Continuous unattended cardiac monitoring (e.g., Holter monitoring) is beyond the scope of this report. Pre-hospital (in ambulance) monitoring and transmission, as well as monitoring solely for the purpose of detecting device failure, are also beyond the scope of this report.

The patient population of interest in this report consists of patients with suspected cardiac arrhythmias manifesting through symptoms such as syncope, presyncope, dizziness, palpitations, and other symptoms that could be attributed to arrhythmia. Patients with life-threatening arrhythmias would not be considered candidates for these

technologies. Patients with primary non-cardiac diagnoses (e.g., epilepsy) are beyond the scope of this report.

Fryback and Thornbury proposed a six-tiered hierarchical model of efficacy for diagnostic technologies.(4) This model can be used as a conceptual guide to identify the primary questions of interest in this report. The six levels are:

- Level 1 – Technical efficacy
- Level 2 – Diagnostic accuracy efficacy (diagnostic yield, accuracy, sensitivity and specificity)
- Level 3 – Diagnostic thinking efficacy (percentage of patients where the test was helpful in making a diagnosis)
- Level 4 – Therapeutic efficacy (percentage of patients where diagnosis led to a change in patient management (change in therapy, avoidance of therapy)
- Level 5 – Patient outcome efficacy (percentage of patients improved with test compared to without test)
- Level 6 – Societal efficacy (Cost-effectiveness analysis from societal viewpoint)

In this report, the questions on efficacy (Key Questions 3-5) are addressing levels 4 and 5 in Fryback and Thornbury's model. We note that much of the literature on remote cardiac monitoring technologies addresses levels 2 and 3, which were not outcomes of interest in this report.

BACKGROUND

In this section, we provide background information on remote cardiac monitoring devices. The purpose of this section is to provide context for the research syntheses presented later in this report. The information presented in this section may be based upon opinion and we have not critically assessed its accuracy. This section is therefore not, in the strictest sense of the term, evidence-based. Consequently, no statement in this *Background* section should be interpreted as an endorsement or a criticism by ECRI Institute.

Cardiac Arrhythmias

Cardiac arrhythmias are irregularities in the heart's natural rhythm, categorized by the site of origin of the defect as well as the rate of the arrhythmia. Ventricular arrhythmias occur in the ventricles, while supraventricular arrhythmias occur mainly in the atria or, less frequently, other structures above the ventricles (such as the atrioventricular node). A very slow heart rate (<60 beats/minute) is known as bradycardia, while a very fast heart rate (>100 beats/minute) is known as tachycardia.

The most serious category of arrhythmia is fast, uncoordinated beats known as fibrillation, which result from the contractions of individual heart muscle fibers rather than the coordinated sequence of muscle fiber contractions of a normal heart beat. Atrial fibrillation is the most common problematic cardiac arrhythmia, with an estimated prevalence of 3% to 5% in the U.S. It develops most often in people over age 65, with a doubling in prevalence with each advancing decade (from 0.5% at age 50-59 years to almost 9% at age 80-89).(5,6) Although atrial fibrillation increases the risk of stroke (see below), it is less serious than ventricular fibrillation, a life-threatening condition where the ventricles cannot pump blood to the body.

Cardiac arrhythmias can be asymptomatic, but they can also cause symptoms such as palpitations, chest pain, dyspnea, dizziness or syncope (a transient loss of consciousness). Syncope is responsible for about 1% of emergency room visits and is

the sixth most common cause of hospital admissions for patients over 65 years.(7) It has been estimated that the general prevalence of syncope is 19% in the general population over 45 years of age.(8) The direct cause of syncope is a sudden loss or cessation of cerebral blood flow, from which recovery is usually rapid and spontaneous. However, in up to 47% of cases, syncope cannot be explained even after a history, physical exam, and conventional testing (i.e., Holter monitoring, tilt table testing).(9) Arrhythmia-mediated syncope is often caused by bradycardias but may also be associated with tachycardias (supraventricular or ventricular), high-grade atrioventricular (AV) block, and in some patients, atrial fibrillation and atrial flutter.(10,11) Palpitations usually result from tachycardic arrhythmias including sinus tachycardia, but have also been associated with atrial fibrillation or atrial flutter.(12,13) Dizziness can be caused by bradycardias or tachycardias.(5)

Some arrhythmias can also lead to more serious adverse events. Atrial fibrillation increases the risk of clot formation and subsequent stroke; it is estimated to be the cause of 24% of strokes in patients aged 80 to 89 years.(6) Ventricular tachycardia can lead to sudden cardiac death in some patients, particularly those with long QT syndrome or cardiomyopathy (ischemic or non-ischemic). Ventricular fibrillation will lead to sudden cardiac death if normal rhythm is not restored within three to five minutes.(5) In some cases, these events occur without warning in previously asymptomatic patients.

Because cardiac rhythm abnormalities can lead to serious events, detection and diagnosis of arrhythmias is important for prevention of such events. Successful diagnosis will allow the patient to receive appropriate treatment to reduce or eliminate the arrhythmia. However, cardiac arrhythmias are sometimes difficult to detect and diagnose, particularly when the arrhythmia occurs infrequently or if it is asymptomatic. These arrhythmias do not fall into any single major category; many types of arrhythmias can be asymptomatic or infrequent (bradycardias, tachycardias, atrial fibrillation, etc.). In such cases, patients deemed at risk for arrhythmic events may require ambulatory electrocardiographic (ECG) monitoring for extended time periods.

Remote Cardiac Monitoring

Remote cardiac monitoring technologies have been developed to allow home ECG monitoring of patients with suspected cardiac arrhythmias or at risk for developing arrhythmias (indications for cardiac monitoring are described in detail under Key Question 2). Various devices are worn externally or implanted, and may record continuously or intermittently. The first ambulatory ECG monitoring system was the Holter monitor, which can record ECG waveforms continuously for up to 72 hours. Since this is insufficient time to diagnose some patients with infrequent arrhythmias, alternative systems have been developed that allow longer monitoring periods. These alternative systems also can transmit ECG data over telephone lines to a remote monitoring center, allowing monitoring personnel faster access to the data. Intermittent-recording non-implantable devices are worn for up to 30 days, and different models record automatically or when activated by the patient during symptoms. By contrast, intermittent-recording implantable or insertable devices may be used for more than a year for remote monitoring of patients, after which the devices are surgically removed. More recently, real-time attended monitoring systems have been developed which record ECGs continuously over long periods of time.(14) For further information regarding different types of remote cardiac monitoring systems, see Key Question 1 in the *Evidence Synthesis* section of this report.

Clinical Practice Guidelines

Information concerning relevant clinical guidelines appears in the *Evidence Synthesis* section of this report under Key Question 2.

Previous Systematic Reviews

Our searches did not identify any previous systematic reviews of remote cardiac monitoring devices.

Ongoing Trials

Our searches identified two ongoing trials related to the technologies evaluated in this report. These trials are described in detail below.

The Eastbourne Syncope Assessment Study II (EaSyAS II) is a randomized controlled trial (RCT) sponsored by Transoma Medical (Minneapolis, MN, USA) with a total enrollment of 240 patients with unexplained syncope. The purpose of the study is to determine whether the cause of syncope can be diagnosed faster with the Sleuth implantable loop recorder (ILR) than with conventional management. The trial will have four separate comparison arms: ILR plus followup at syncope clinic, ILR plus routine followup, conventional care plus followup in syncope clinic, and conventional care plus routine followup. The trial is being conducted at Eastbourne General Hospital in East Sussex, United Kingdom. The start date of the study was August 2007, and the expected completion date is August 2009.(15)

A randomized trial of atrial fibrillation rate control therapy guided by continuous ambulatory monitoring was also identified. This study has a listed completion date of August 2006, but to our knowledge the data have not yet been published in a peer-reviewed journal. The study enrolled 45 patients with atrial fibrillation to compare a standard rate-control strategy with one using the CardioNet mobile cardiac outpatient telemetry device to guide therapy for the management of atrial fibrillation. Both patient groups received the Cardionet device, but the treating physician in the standard rate-control group was blinded to the ECG reports from the CardioNet device. This study was conducted at Beth Israel Deaconess Medical Center (Boston, MA) and was sponsored by CardioNet (San Diego, CA).(16)

Regulatory Issues

Manufacturers and U.S. Food and Drug Administration (FDA) Status

The list of manufacturers of remote cardiac monitoring devices is extensive, and the list of devices is even more extensive. A list of manufacturers and devices that have received Food and Drug Administration (FDA) approval (exceptions are noted) can be found in Table C-1, Appendix C. The general indications for remote cardiac monitoring devices are discussed under Key Question 2.

Since real-time continuous attended monitors are a class of device that are less-well studied than patient/event-activated intermittent recorders, we present the complete indications/contraindications stated in the FDA labeling for these devices.

The CardioNet mobile cardiac outpatient telemetry (MCOT) system is manufactured by CardioNet (San Diego, CA). In February 2002, CardioNet received FDA 510(k) marketing approval for the CardioNet Ambulatory Monitor with Arrhythmia Detection (an updated 510(k) approval was obtained in October 2006).(17) The HEARTLink II ECG arrhythmia detector and alarm system is manufactured by Cardiac Telecom Corporation (Greensburg, PA). In November 1998, Cardiac Telecom received FDA 510(k) marketing approval for the HEARTLink II system.(1) These are the only remote monitoring devices approved by the FDA with Product Code DSI Classification, Arrhythmia Detector and Alarm. These devices have the following indications for use.

Indications for use:

- Patients who have demonstrated a need for cardiac monitoring and are at low risk of developing primary ventricular fibrillation or sustained ventricular tachycardia.
- Patients with dizziness or lightheadedness
- Patients with palpitations
- Patients with syncope of unknown etiology
- Patients who require monitoring for non life-threatening arrhythmias, such as atrial fibrillation, other supraventricular arrhythmias, evaluation of various

bradyarrhythmias and intermittent bundle branch block. This includes postoperative monitoring for these rhythms.

- Patients recovering from coronary artery bypass graft (CABG) surgery who require monitoring for arrhythmias
- Patients requiring monitoring for arrhythmias inducing co-morbid conditions such as hyperthyroidism or chronic lung disease
- Patients with obstructive or central sleep apnea to evaluate possible nocturnal arrhythmias
- Patients requiring arrhythmia evaluation for etiology of stroke or transient cerebral ischemia, possibly secondary to atrial fibrillation

In addition, the 2006 FDA approval document for the CardioNet MCOT system includes the following indications:

- Data from the device may be used by another device to analyze measure or report QT interval. The device is not intended to sound any alarms for QT interval changes
- Patients who require monitoring of effect of drugs to control ventricular rate in various atrial arrhythmias (e.g. atrial fibrillation)

The CardioNet MCOT system also lists the following contraindications:

- Patients with potentially life-threatening arrhythmias who require inpatient monitoring
- Patients who the attending physician thinks should be hospitalized(18)

Specific contraindications to use were not stated in the FDA approval document for the Heartlink II system.(1)

The VST^3 (Vital Signs Recorder and Transmitter) is manufactured by Biowatch Medical (Columbia, SC). In September 2004, Biowatch Medical received FDA 510(k) marketing approval for the VST^3. This device is indicated for use to monitor adults with abnormal heart rhythms and other symptoms of cardiac disease, such as:

- Arrhythmia and dysrhythmia
- Skipped beats or pauses

- Rapid, slow, or irregular heart rate
- Lightheadedness or faintness
- Palpitations

The device is not intended to sound any alarms. Contraindications to use were not stated in the FDA approval document.(19)

The CG-6108 Continuous ECG Monitor and Arrhythmia Detector system is manufactured by Card Guard Scientific Survival Ltd. (Rehovot, Israel). In August 2006, Card Guard received FDA 510(k) marketing approval for the CG-6108 system. The device is also marketed as the Lifestar Ambulatory Cardiac Telemetry (ACT) by Life Watch (Buffalo Grove, Il). This device is indicated for use by patients who experience transient symptoms that may suggest cardiac arrhythmia. Contraindications to use were not stated in the FDA approval document.(3)

Current CMS Policy Regarding Remote Cardiac Monitoring

Current CMS policy appears in the *NCD for Electrocardiographic Services* (20.15).(20) The benefit category is listed as Diagnostic Tests (other). The CMS ambulatory electrocardiographic services framework currently includes patient/event-activated intermittent recorders (attended and non-attended) and non-activated continuous recorders (non-attended).

METHODS

Key Questions Addressed

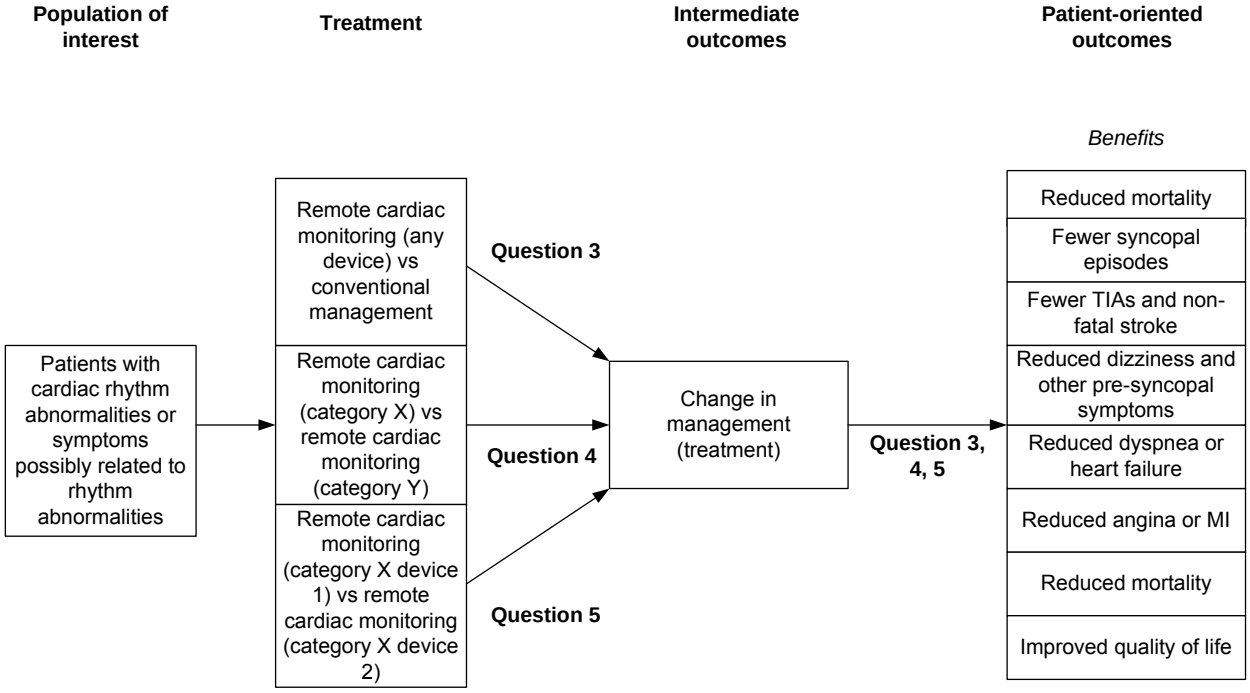
We address the following Key Questions in this report:

1. What types of devices/techniques are currently available to remotely assess cardiac rhythm abnormalities in ambulatory patients?
2. How is patient eligibility for remote cardiac monitoring (1.a and b) determined?
3. Is management changed based on information obtained from remote cardiac monitoring using any of the identified categories of devices and do these changes lead to improvements in the following outcomes in ambulatory patients (or a subgroup of ambulatory patients)?
    a. Palpitations
    b. Syncopal episodes
    c. TIAs and non-fatal stroke
    d. Dizziness and other pre-syncopal symptoms
    e. Dyspnea and heart failure
    f. Angina and MI
    g. Mortality
    h. Quality of life
4. Of the patient outcomes for which improvements have been demonstrated, do any categories of devices (as listed under Question 1) lead to greater improvement in these outcomes in ambulatory patients (or a subgroup of ambulatory patients) compared to any of the other categories of devices?
5. Of the patient outcomes for which improvements have been demonstrated, do any devices within a category lead to greater improvement in these outcomes in ambulatory patients (or a subgroup of ambulatory patients) compared to any of the other devices within the same category?
6. What accreditation standards exist for training and continuing education for the interpretation of data from remote cardiac monitoring?
7. What standards exist to guide how data gathered from remote cardiac monitors should be incorporated into a patient's continuum of care? In practice (i.e., as reported in the published literature, "gray literature," etc.), what are the

characteristics of the patient care infrastructure using remote cardiac monitoring (e.g., use of either attending technicians or attending physicians) and how are the data gathered from remote cardiac monitoring used to inform patients' continuum of care?

Figure 1 illustrates the relationship between remote cardiac monitoring, the Key Questions, and the outcomes of interest. Because Key Questions 1, 2, 6, and 7 are not evidence-based, they are not included in Figure 1. This report focuses primarily on patient-oriented outcomes (see list under Key Question 3). One intermediate outcome (change in management) has also been included. Diagnostic outcomes, such as diagnostic accuracy or yield, are beyond the scope of this report.

Figure 1. Analytic Framework



Literature Searches

Details of our literature searches, which included searches of 16 electronic databases, hand searches of the bibliographies of all retrieved articles, and searches of the gray literature, are presented in Appendix A.

Study Inclusion/Exclusion Criteria

General Inclusion/Exclusion Criteria

We used the following general criteria to determine which studies would be included in our analysis for Key Questions 3 through 5:

1. Studies must have been published in English. We recognize the possibility that requiring studies to be published in English could lead to bias, but we believe it is sufficiently unlikely that we cannot justify the additional time and expense for translation.(22,23)
2. Studies must have addressed one of the Key Questions.
3. If the same study is reported in multiple publications, only the most complete publication will be included. This serves to avoid duplication of data. Overlapping publications will be included if they present additional data not available in the most complete publication.
4. For controlled studies, 10 or more patients per treatment group must have relevant outcome data reported. For uncontrolled studies, 10 or more patients must have relevant outcome data reported. This increases the likelihood that the studies contain a representative sampling of the patient population.

Question-Specific Inclusion/Exclusion Criteria

The following inclusion/exclusion criterion was specific to Key Questions 1 and 7:

- Any publication type, including review articles, FDA approvals, meeting abstracts, Web-based publications and other "gray literature" will be used to identify other methods of remote cardiac monitoring

The following inclusion/exclusion criterion was specific to Key Questions 2 and 6:

- Clinical practice guidelines, published standards and position papers will be reviewed for recommendations on patient selection criteria.

The following inclusion/exclusion criterion was specific to Key Questions 3, 4, and 5:

- Studies published as full journal articles will be utilized for any quantitative analyses. Meeting abstracts from professional meetings relevant to telecardiology presented during the past two years will be reviewed and described but not analyzed.

The following inclusion/exclusion criterion was specific to Key Question 3:

- Before-and-after uncontrolled studies will be included in addition to controlled trials. Information from before-and-after studies will be tabled, but not analyzed unless the total follow-up period is at least 12 months in duration. The exception to this rule is the outcome change in disease management, as many patients undergo a change in management in a time frame well under 12 months. For this outcome, we will analyze before-after study data regardless of follow-up time. The second rule for analysis is that patients in before-and-after studies must have undergone prior non-diagnostic Holter monitoring and/or tilt table testing before entering the study. This increases the likelihood that the patients would not be diagnosed during further conventional management.

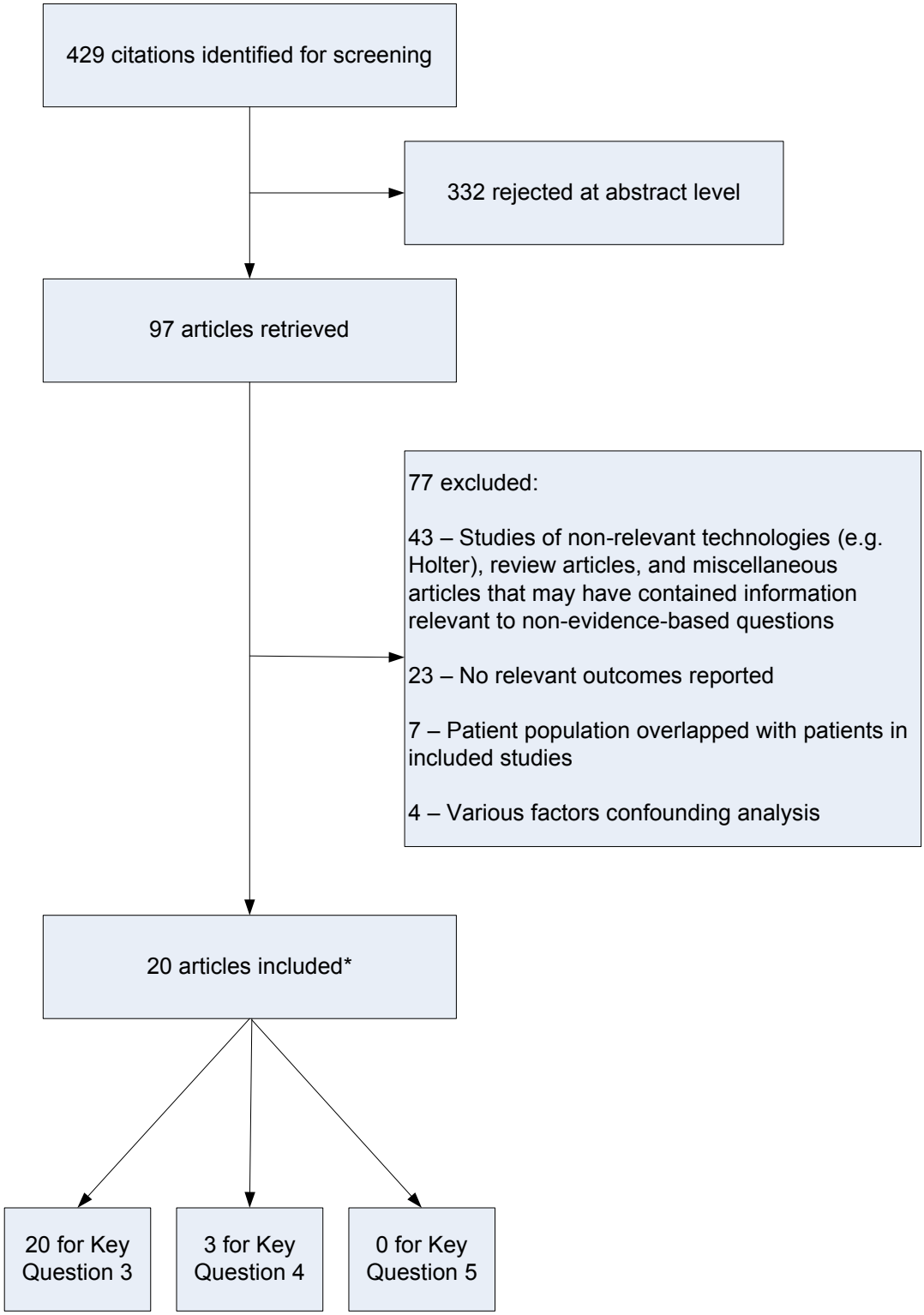
The following inclusion/exclusion criterion was specific to Key Questions 4 and 5:

- Only controlled studies will be included. Controlled studies are required in situations where influences other than the technology of interest may be responsible for treatment outcomes. Comparison of one type of remote cardiac monitoring to a control group monitored using another device is needed to sort out the influence of the monitoring technology from other potential influences. Trials that compare two monitoring technologies in the same patients cannot be used to determine which technology leads to better clinical outcomes. Therefore, only trials with head-to-head comparisons of one type of monitoring to another or one device to another will be considered.

Identification of Evidence Base

The selection process used to identify the articles that comprise the evidence base for the Key Questions addressed in this report is presented in Figure 2. Our searches identified 429 articles that potentially addressed Key Questions 3 through 5. Of these 429 articles, we retrieved 97. Twenty included articles addressed Key Question 3 (although only 17 were used in the analysis), three included studies addressed Key Question 4, and no included articles addressed Key Question 5. The included studies are listed in the *Evidence Synthesis* section under each Key Question that they address. Key Questions 1, 2, 6, and 7 did not involve an evaluation of evidence; therefore, we do not include them as part of the selection process in Figure 2.

Figure 2. Summary of Study Selection Process



*Three studies addressed both Key Question 3 and Key Question 4

Data Extraction

Information extracted from the included studies is presented in evidence tables in Appendices D-F. These tables describe patient inclusion/exclusion criteria, information on enrolled patients (demographics, underlying risk, etc.), design details (randomization, blinding, etc.) and study results. When study authors did not report dichotomous data as percentages, we computed percentages. We have only extracted outcome data relevant to the Key Questions in this report.

Evaluation of Individual Study Quality

A poorly designed study may contain biases that may make a treatment look more or less effective than it actually is. In well-designed studies, the outcomes can be definitively attributed to the intervention of interest.

In order to grade the quality of studies, we use quality rating scales specific for different study designs. These scales allow us to calculate an evidence quality score based on *a priori* quality criteria. The questions in the scales are worded so that study design aspects that provide evidence with good internal validity result in “Yes” answers, design aspects that create potential for bias result in “No”, and design aspects that are inadequately described result in an answer of “NR” (not reported).

Since the studies identified for the evidence base included both controlled trials and uncontrolled single-arm studies, we used two different quality scales for the differing study designs. A 25-item scale was used to assess the quality of controlled trials, and an 11-item scale was used to assess the quality of single-arm studies. The complete scales and details of the scoring system appear in Appendix B.

Evaluation of the Strength of the Evidence

ECRI Insitute's system, which is presented in Appendix B, provides systematic, reproducible, transparent, and *a priori* decision rules for rating the strength of a body of evidence.(24) In applying the system, we draw a distinction between a qualitative conclusion (one which answers the question "Does it work?") and a quantitative conclusion (one which answers the question "How well does it work?"). Second, we utilize a system that we developed to assign a strength rating to the evidence that supports our qualitative conclusions and a rating that defines how stable we believe any estimate of treatment effect to be.

Table 1 presents definitions of the strength of evidence and stability ratings that may be obtained using the system. These definitions, which are similar to those proposed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group,(25) are intuitive. Qualitative conclusions that are supported by strong evidence are less likely to be overturned by the publication of new data than are conclusions supported by weak evidence. Likewise, quantitative estimates of treatment effect that are backed up by stable data are less likely to change significantly when new data are published than are estimates of treatment effect drawn from a less stable data set. For more information on the criteria used to rate studies, see the *Quality of Included Studies* section under each Key Question in the *Evidence Synthesis* section of the report.

Table 1. Interpretation of Strength of Evidence and Stability Ratings

Strength of Evidence Interpretation	
Qualitative Conclusion (Does it work?)	
Strong evidence	Evidence supporting the qualitative conclusion is convincing. It is highly unlikely that new evidence will lead to a change in this conclusion.
Moderate evidence	Evidence supporting the qualitative conclusion is somewhat convincing. There is a small chance that new evidence will overturn or strengthen our conclusion. ECRI recommends regular monitoring of the relevant literature at this time.
Weak evidence	Although some evidence exists to support the qualitative conclusion, this evidence is tentative and perishable. There is a reasonable chance that new evidence will overturn or strengthen our conclusions. ECRI recommends frequent monitoring of the relevant literature at this time.
Inconclusive	Although some evidence exists, this evidence is not of sufficient strength to warrant drawing an evidence-based conclusion from it. ECRI recommends frequent monitoring of the relevant literature at this time.
Quantitative Conclusion (How well does it work?)	
High stability	The estimate of treatment effect included in the conclusion is stable. It is highly unlikely that the magnitude of this estimate will change substantially as a result of the publication of new evidence.
Moderate stability	The estimate of treatment effect included in the conclusion is somewhat stable. There is a small chance that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI recommends regular monitoring of the relevant literature at this time.
Low stability	The estimate of treatment effect included in the conclusion is likely to be unstable. There is a reasonable chance that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI recommends frequent monitoring of the relevant literature at this time.
Unstable	Estimates of the treatment effect are too unstable to allow a quantitative conclusion to be drawn at this time. ECRI recommends frequent monitoring of the relevant literature.

We apply each kind of rating to the *body* of evidence that addresses each outcome, not to individual studies. We also rate on an outcome-by-outcome basis. Four primary factors determine our ratings for both strength and stability; the quality, quantity, robustness, and consistency of the evidence. Under certain circumstances, the size of the treatment's effect and whether multicenter trials are available also influence our ratings of the evidence underlying qualitative conclusions.

Statistical Methods

Whenever relevant data from three or more studies were available and could be combined (determined after assessment of clinical and methodological diversity), we summarized the results using meta-analysis. Meta-analysis allows one to pool data

from different studies to obtain an average estimate of the treatment effect on a given outcome. It also provides a means for formally identifying and exploring important differences among the results of different studies (consistency).

In brief, we first tested the available data to determine whether the results of the studies included in the meta-analysis differed from one another by more than that expected by chance (statistical heterogeneity testing) using the I^2 statistic ($I^2 \geq 50\%$ indicates notable unexplained inconsistency).(26) If study results did not differ in this manner (i.e., the data were consistent), we next pooled the study results in a random-effects model to obtain a summary estimate.(27) We calculated individual study effect sizes from dichotomous data using the log odds ratio (summary log odds ratios were converted to odds ratios in the text and conclusion statements). The method used to calculate effect size (Hedges' d) for continuous data was described by Cooper and Hedges.(28) If results across studies revealed unexplained inconsistency, a random-effects meta-analysis was used to reach a qualitative conclusion only (no summary estimate of the effect size was presented).

For outcomes with only one or two available controlled trials, we used a best-evidence approach to incorporate data from before-after single-arm studies in our analysis. This required imputation of a control group for each single-arm study, with an assumed rate of improvement based on the control group(s) from the controlled trials.

Having obtained a summary estimate of the results, we then tested the robustness of our findings using sensitivity analyses as recommended by Olkin.(29) This involved the systematic addition of each study (cumulative meta-analysis) to determine the study's effect on the summary result. If a quantitative summary estimate could be obtained, cumulative random-effects meta-analysis (by publication date) was used for testing quantitative robustness (for additional details of quantitative robustness testing, see Appendix B). We also removed each individual study separately to see if the quantitative conclusion could be overturned. To test qualitative robustness, we used the same sensitivity analyses described above to see if the qualitative conclusion could be overturned. If the qualitative estimate was based on imputation of hypothetical control groups, we performed an additional sensitivity analysis (assuming a control group success rate three times higher than our best estimate).

EVIDENCE SYNTHESIS

Key Question 1: What Types of Devices/Techniques Are Currently Available to Remotely Assess Cardiac Rhythm Abnormalities in Ambulatory Patients?

This question requires a summary of the technologies currently used to measure remote cardiac monitoring. The information described in this section is derived primarily from review articles written by experts in the field, FDA approval documents, and manufacturer Web sites.

Summary of Technologies Used for Remote Cardiac Monitoring

A variety of techologies are currently used for remote cardiac monitoring in ambulatory patients. These devices can be categorized according to whether they monitor cardiac rhythm intermittently or continuously, and whether they are worn externally or implanted. Each method and its advantages and limitations are described below.

Patient/Event-Activated Intermittent Recorders

Devices in this category monitor ECGs but do not continuously record data. Data can be transmitted over the phone to a doctor's office, clinic, or hospital (some devices also can upload data to a PC). The major advantage of these devices relative to Holter monitors is that they allow ECG monitoring for longer time periods. Remote monitoring centers can provide attended monitoring services (using technicians or other medical personnel) for these devices; Independent Diagnostic Testing Facilities (IDTF) are an important provider of these services.(30)

These devices can be further subcategorized as externally-worn or implantable, whether they have memory loop-recording capability, and whether they offer both automatic and patient-triggered transmission of monitoring data or only patient-activated transmissions. The different subcategories are described below.

Pre-symptom Memory Loop Cardiac Event Recorders (External Loop Recorders)

Standard external loop recorders (ELRs)

The standard ELR records several minutes of activity at a time and then starts over, a process referred to as memory loop recording. The patient activates this device to record when a symptom occurs and then data from the device is typically transmitted to monitoring centers for immediate review. This process is repeated whenever symptoms occur over a period of 20 to 30 days (which is the typical amount of time the device is worn by the patient). Since the data that are recorded by the device are typically associated with a symptom, a physician can also determine whether that symptom is a result of a cardiac arrhythmia. When a patient experiences the symptoms of an event, he or she holds the device next to his or her chest and activates the device to begin recording. However, due to the need for the patient to signal an event, the standard cardiac event monitor typically only captures events associated with a patient's symptoms and not those events that are asymptomatic.(31)

Auto-trigger external loop recorders (ELRs)

The auto-trigger ELR also memory loop records, capturing several minutes of heart activity at a time before starting over. In addition, however, the auto-trigger ELR uses systems to automatically detect events that may not be associated with a patient experiencing symptoms. Unlike a standard ELR, an auto-trigger ELR does not rely on the patient's ability to activate it and, as a result, is able to capture asymptomatic events in addition to symptomatic ones. However, the auto-trigger device still relies on the patient to call in and transmit the event by reaching the physician or a technician at a physician's office or a monitoring center and holding the cardiac event monitor up to a telephone to transmit the event data.(31)

Pre-symptom Memory Loop Cardiac Event Recorders (Implantable or Insertable Loop Recorders)

Implantable or insertable loop recorders (ILRs) perform the same function as ELRs, except that they are implanted subcutaneously in the left or right chest region. The main difference between ILRs and ELRs is that ILRs can be used for a much longer time period (current models offer 14-20 months of longevity) before being surgically

removed. Currently, the only commercially-available ILRs are the Reveal® Plus (Medtronic) and the Sleuth™ (Transoma Medical), both of which can be programmed for automatic activation or patient activation (Reveal®, the earlier model of Reveal® Plus, allowed only patient activation).(32) Unlike Reveal® Plus, which cannot transmit ECG data from home, Sleuth is a wireless system which can transmit ECG data to a remote monitoring center.(33)

Post-symptom Event Recorders

Post-symptom event monitors are hand-held devices that have no chest electrodes. These monitors lack the memory loop of pre-symptom recorders and can therefore only record the rhythm that occurs after being triggered by the patient. They generally do not have automatic activation upon occurrence of asymptomatic arrhythmias.

Limitations

Whether loop recorders or post-event recorders, devices that are exclusively patient-activated will only identify arrhythmias associated with symptomatic events (that can be perceived by the patients). Furthermore, because some patients have difficulty activating a recorder when they experience symptoms, patient-activated devices will not even capture all symptomatic events.(34-36) In contrast, automatic event-activated recorders will capture asymptomatic and symptomatic arrhythmias and are thus free from the limitations described above.(13,36)

However, automatic recorders have disadvantages as well. They may activate unnecessarily (false event) or not record during some symptomatic events, depending on the predetermined rhythm specifications that lead to device activation. Also, the limited memory of automatic recorders may result in a false event erasing a prior-recorded true event.(37) Less memory also means that more frequent downloads or transmissions are required for multiple recorded events.

Pre-symptom looping devices that can record ECGs immediately before and after an event have an advantage over post-symptom recorders, as the arrhythmia may have ended by the time the post-event recorder is activated. For this reason, patients whose primary symptom is syncope are unlikely to be diagnosed by post-symptom recorders.

However, because external looping devices require patch electrodes to be attached to the skin on a daily basis, they are less comfortable to wear than post-event recorders.(13) Thus, patients may be less compliant with wearing and maintaining ELRs. The number of electrodes required might also affect compliance, as more electrodes tend to produce more discomfort for the patient. Patch electrodes can also come loose from the skin and thus fail to record events.

Although ILRs allow longer monitoring periods than other devices, they have other limitations. First, the patient must undergo a procedure for device implantation. Second, ELRs and post-event recorders usually allow transmission of ECG data transtelephonically or through a PC to a receiving center or doctor's office, while ILR data from the Reveal® Plus device can only be accessed during office visits (the newer Sleuth™ device allows home transmission of ECG data and thus does not have this limitation). Furthermore, our searches identified a case report of interference by a cellular telephone with an ILR when the phone was placed over the subcutaneous pocket containing the ILR. The artifact produced by the telephone ringing was automatically recorded and stored in the ILR's memory.(38) One study mentioned that older patients had more difficulties activating the ILR after syncope and consulting promptly after a syncopal event,(34) although the relevant data were not presented and this observation has not been confirmed in other studies.

Real-Time Continuous Attended Remote Cardiac Monitoring

Real-time continuous attended remote cardiac monitoring systems automatically record and transmit arrhythmic event data from ambulatory patients to personnel monitoring, or attending the monitor, at a clinic or hospital. Four such systems are commercially marketed at present: The CardioNet system (CardioNet, Inc), the HEARTLink II system (Cardiac Telecom Corp), the VST™ (Vital Signs Transmitter, Biowatch Medical), and the CG-6108 continuous ECG monitor, also known as the Lifestar ambulatory cardiac telemetry (ACT) system (Card Guard Scientific Survival Ltd.).(1-3,39) These systems allow automatic wireless transmission of abnormal ECG waveforms at the time of event occurrence from the patient's home to an attended monitoring center. As noted earlier, the CardioNet system and the HEARTLINK II system are the only remote monitoring

devices approved by the FDA with Product Code DSI Classification, Arrhythmia Detector and Alarm. In addition, the CardioNet system has a built-in cellular telephone that automatically transmits arrhythmic signals to the monitoring center when the patient is away from home (the HEARTLink II system can only transmit signals from a base station in the patient's home; limitations of the VST^{TM} and CG-6108 are unclear based on published information).(2)

This technology was developed to overcome the limitations of other remote cardiac monitoring technologies. Patient-activated event recorders are non-continuous and insufficient for patients who have difficulty triggering monitoring equipment. Although many event recorders have automatic activation capability, and allow the patient to transmit data to a receiving station, they do not automatically transmit the event data at the time of occurrence to an attended monitoring station. The ability to respond immediately when clinically important events occur is the major advantage of real-time continuous attended monitoring systems.

A detailed description of specific devices within each category appears in Table C-1, Appendix C. Thirty-one devices were ELRs, two devices were ILRs, 17 devices were post-event recorders, Four devices were real-time continuous attended monitors, and three devices had characteristics of more than one of these categories.

Subsection Summary

Several devices are currently used to remotely assess cardiac rhythm abnormalities in ambulatory patients. The largest category of devices includes patient/event-activated intermittent recorders (pre-symptom continuous loop and post-symptom recorders). Within this broad category, ELRs (patient and/or event-activated) are the largest subcategory, with 31 identified devices. Real-time continuous attended remote cardiac monitoring is the newest category, with four commercially-available devices.

Key Question 2: How is Patient Eligibility for Remote Cardiac Monitoring Determined?

Our searches identified clinical practice guidelines, published standards and position papers that addressed this question. Below we describe patient characteristics (Section A) and other factors (Section B) for determining patient eligibility.

A. Patient Characteristics

Guidelines for Ambulatory Electrocardiography (AECG)

Two references addressed AECG use in the United States and two other references describe guidelines outside the United States.

United States

The American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) published guidelines in 2006 for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death practice guidelines.(40) These guidelines reported the following indications for use of AECG:

Class I – Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.

- Ambulatory ECG is indicated when there is a need to clarify the diagnosis by detecting arrhythmias, QT-interval changes, T-wave alternans, or ST changes, to evaluate risk, or to judge therapy (Level of evidence: A).

- Event monitors are indicated when symptoms are sporadic to establish whether they are caused by transient arrhythmias (Level of evidence: B).

- Implantable recorders are useful in patients with sporadic symptoms suspected to be related to arrhythmias such as syncope when a symptom-rhythm correlation cannot be established by conventional diagnostic techniques (Level of evidence: B).

The guidelines also state that “the use of continuous or intermittent ambulatory recording techniques can be very helpful in diagnosing a suspected arrhythmia, establishing its frequency, and relating symptoms to the presence of the arrhythmia. Silent myocardial ischemic episodes may also be detected.”(40)

The text of the full guidelines does make some distinction between continuous monitoring for 24-48 hours with a Holter monitor and intermittent monitoring with event monitors (external or implanted).(41) The guidelines state that “a 24 to 48 h continuous Holter recording is appropriate whenever the arrhythmia is known or suspected to occur at least once a day. For sporadic episodes producing palpitations, dizziness, or syncope, conventional (externally-worn) event monitors are more appropriate because they can record over extended periods of time.” No distinction is made between ELRs and post-event recorders, or patient-activated versus automatic-activated devices. The guidelines also mention that ILRs “have been shown to be extremely useful in diagnosing serious tachyarrhythmias and bradycardias in patients with life-threatening symptoms such as syncope.” However, the text does not provide clear indications for when ILRs should be used instead of ELRs.

The guidelines make no reference to real-time continuous attended monitoring systems or indications for use of such systems.

The ACC/AHA guidelines for ambulatory electrocardiography (published in 1999) presented the following indications related to AECG, but do not provide separate indications for different categories of AECG monitoring devices (Table 2).(42)

Table 2. ACC/AHA Guidelines for Ambulatory Electrocardiography

ACC/AHA Guidelines for Ambulatory Electrocardiography (1999)(42)
AECG to assess symptoms possibly related to rhythm disturbances
Class I • Patients with unexplained syncope, near syncope, or episodic dizziness in whom the cause is not obvious. • Patients with unexplained recurrent palpitation.
Class IIb • Patients with episodic shortness of breath, chest pain, or fatigue that is not otherwise explained. • Patients with neurological events when transient atrial fibrillation or flutter is suspected. • Patients with symptoms such as syncope, near syncope, episodic dizziness, or palpitations in whom a probable cause other than an arrhythmia has been identified but in whom symptoms persist despite treatment of this other cause.
Class III • Patients with symptoms such as syncope, episodic dizziness, or palpitations in whom other causes have been identified by history, physical examination, or laboratory tests. • Patients with cerebrovascular accidents, without other evidence of arrhythmia.
Indications for AECG Arrhythmia detection to assess risk for future cardiac events in patients without symptoms from arrhythmia
Class I • None.
Class II b • Post-MI patients with LV dysfunction (ejection fraction ≤40%) • Patients with CHF • Patients with idiopathic hypertrophic cardiomyopathy
Class III • Patients who have sustained myocardial contusion • Systemic hypertensive patients with LV hypertrophy • Post-MI patients with normal LV function • Preoperative arrhythmia evaluation of patients for noncardiac surgery • Patients with sleep apnea • Patients with valvular heart disease

ACC/AHA Guidelines for Ambulatory Electrocardiography (1999)(42)
Indications for measurement of HRV to assess risk for future cardiac events in patients without symptoms from arrhythmia
Class I • None
Class IIb • Post-MI patients with LV dysfunction • Patients with CHF • Patients with idiopathic hypertrophic cardiomyopathy
Class III • Post-MI patients with normal LV function • Diabetic subjects to evaluate for diabetic neuropathy • Patients with rhythm disturbances that preclude HRV analysis (ie, atrial fibrillation)
Indications for AECG to assess antiarrhythmic therapy
Class I • To assess antiarrhythmic drug response in individuals in whom baseline frequency of arrhythmia has been characterized as reproducible and of sufficient frequency to permit analysis
Class IIa • To detect proarrhythmic responses to antiarrhythmic therapy in patients at high risk
Class IIb • To assess rate control during atrial fibrillation • To document recurrent or asymptomatic nonsustained arrhythmias during therapy in the outpatient population
Class III • None
Indications for AECG to assess pacemaker and ICD function
Class I • Evaluation of frequent symptoms of palpitation, syncope, or near syncope to assess device function to exclude myopotential inhibition and pacemaker-mediated tachycardia and to assist in the programming of enhanced features such as rate responsivity and automatic mode switching • Evaluation of suspected component failure or malfunction when device interrogation is not definitive in establishing a diagnosis • To assess the response to adjunctive pharmacological therapy in patients receiving frequent ICD therapy
Class IIb • Evaluation of immediate postoperative pacemaker function or ICD implantation as an alternative or adjunct to continuous telemetric monitoring • Evaluation of the rate of supraventricular arrhythmias in patients with implanted defibrillators

ACC/AHA Guidelines for Ambulatory Electrocardiography (1999)(42)
Class III • Assessment of ICD/pacemaker malfunction when device interrogation, ECG, or other available data (chest radiography and so forth) are sufficient to establish an underlying cause/diagnosis • Routine followup in asymptomatic patients
Indications for AECG for ischemia monitoring
Class I • None
Class IIa • Patients with suspected variant angina
Class IIb • Evaluation of patients with chest pain who cannot exercise • Preoperative evaluation for vascular surgery of patients who cannot exercise • Patients with known CAD and atypical chest pain syndrome
Class III • Initial evaluation of patients with chest pain who are able to exercise • Routine screening of asymptomatic subjects
Indications for AECG monitoring in pediatric patients
Class I • Syncope, near syncope, or dizziness in patients with recognized cardiac disease, previously documented arrhythmia, or pacemaker dependency • Syncope or near syncope associated with exertion when the cause is not established by other methods • Evaluation of patients with hypertrophic or dilated cardiomyopathies • Evaluation of possible or documented long QT syndrome • Palpitation in the patient with prior surgery for congenital heart disease and significant residual hemodynamic abnormalities • Evaluation of antiarrhythmic drug efficacy during rapid somatic growth • Asymptomatic congenital complete AV block, nonpaced
Class IIa • Syncope, near syncope, or sustained palpitation in the absence of a reasonable explanation and where there is no overt clinical evidence of heart disease • Evaluation of cardiac rhythm after initiation of an antiarrhythmic therapy, particularly when associated with a significant proarrhythmic potential • Evaluation of cardiac rhythm after transient AV block associated with heart surgery or catheter ablation • Evaluation of rate-responsive or physiological pacing function in symptomatic patients

ACC/AHA Guidelines for Ambulatory Electrocardiography (1999)(42)
Class IIb • Evaluation of asymptomatic patients with prior surgery for congenital heart disease, particularly when there are either significant or residual hemodynamic abnormalitites, or a significant incidence of late postoperative arrhythmias • Evaluation of the young patient (<3 years old) with a prior tachyarrhythmia to determine if unrecognized episodes of arrhythmia recur • Evaluation of the patient with a suspected incessant atrial tachycardia • Complex ventricular ectopy on ECG or exercise test
Class III • Syncope, near syncope, or dizziness when a noncardiac cause is present • Chest pain without clinical evidence of heart disease • Routine evaluation of asymptomatic individuals for athletic clearance • Brief palpitation in the absence of heart disease • Asymptomatic Wollf-Parkinson-White syndrome

Class I – Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.

Class II – Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure or treatment.

IIa – Weight of evidence/opinion is in favor of usefulness/efficacy.

IIb – Usefulness/efficacy is less well-established by evidence/opinion

Class III – Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

In 2006, the AHA/American College of Cardiology Foundation (ACCF) published a Scientific Statement on the evaluation of syncope. Although this is not a formal guideline, the document reviewed evidence for diagnostic approaches to syncope. AECG is considered appropriate in patients with syncope who have had a “normal” evaluation (i.e., no underlying heart disease was detected) and the diagnosis remains uncertain. The document states that a Holter monitor is appropriate for episodes that occur at least every day, and event monitoring is ideal for episodes that occur at least once a month. An ILR is considered the most likely technology to identify the mechanism of syncope in patients with unexplained syncope.(43)

GUIDELINES FOR AECG USE OUTSIDE THE UNITED STATES

In 2004, the European Society of Cardiology published guidelines with the following indications for use of ECG monitoring in patients with syncope.(44)

Table 3. European Society of Cardiology Guidelines on Management (Diagnosis and Treatment) of Syncope

European Society of Cardiology Guideline Recommendations – Indications for ECG monitoring
Class I: • Holter monitoring is indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope and very frequent syncopes or presyncopes • When the mechanism of syncope remains unclear after full evaluation, implantable loop recorder (ILR) is indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope or a history of recurrent syncope with injury
Class II: • Holter monitoring may be useful in patients who have the clinical or ECG features suggesting an arrhythmic syncope in order to guide subsequent examinations (i.e., electrophysiological study) • External loop recorder (ELR) may be indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope and inter-symptom interval ≤4 weeks • ILR may be indicated: o In an initial phase of the work-up instead of completion of conventional investigations in patients with preserved cardiac function who have the clinical or ECG features suggesting an arrhythmic syncope o 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
Class III: • ECG monitoring is unlikely to be useful in patients who do not have the clinical or ECG features suggesting an arrhythmic syncope and therefore, it should not be performed

Class I – Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.

Class II – Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure or treatment.

IIa – Weight of evidence/opinion is in favor of usefulness/efficacy.

IIb – Usefulness/efficacy is less well-established by evidence/opinion

Class III – Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

In 2004, the British Columbia Medical Services Commission published guidelines with the following indications for use of AECG monitoring (Table 4).(45)

Table 4. British Columbia Medical Services Commission Guidelines for AECG

British Columbia Medical Services Commission Guidelines for AECG
Recommendation 1 - Patients suitable for ambulatory ECG monitoring: • Ambulatory ECG monitoring is suitable for patients with symptoms which may be caused by arrhythmia, such as palpitations, light-headedness or syncope. Patients should be able to record symptoms in a diary or have symptoms recorded for them.
Recommendation 2 – Choice of ambulatory ECG monitoring: • Patients with symptoms occurring daily or almost daily or those who have syncope without warning may be evaluated with a 24-hour Holter monitor. Patients with symptoms occurring less frequently may be better evaluated using a patient-activated event recorder.
Recommendation 3 – Ambulatory ECG monitoring for complex cardiac conditions: • Ambulatory ECG monitoring is often useful in more complex cardiac conditions. Selection of patients and choice of ambulatory monitor are best discussed with a specialist/cardiologist. The following categories of patients may benefit from ambulatory ECG monitoring: • Patients with clinical suspicion of pacemaker malfunction when this cannot be determined by routine ECG and analysis by the manufacturer's programmer. • Patients with frequent, reproducible cardiac arrhythmias who are using antiarrhythmic drugs and who need to undergo serial monitoring to assess response or adverse reactions to drug therapy. • Patients being assessed for trends in heart rate, e.g., drug therapy in atrial fibrillation, relative bradycardia.
Recommendation 4 – Patients not recommended for ambulatory ECG monitoring: • The following categories of patients are not recommended for ambulatory ECG monitoring: • Patients with organic heart disease who are at immediate risk of life-threatening arrhythmia, injury, or sudden death, or patients with arrhythmias causing ischemic chest pain, pulmonary edema, etc. These patients require emergency assessment. • Patients with symptoms such as chest pain which may be due solely to coronary artery disease. Other investigations such as stress testing are more reliable for diagnosing coronary artery disease. • Asymptomatic patients with recent myocardial infarction.

The Cardiac Society of Australia and New Zealand lists the following indications for AECG:(46)

- “The major indications for ambulatory electrocardiographic monitoring are in patients in whom the probable mechanism of palpitations is not clear from clinical history and in patients with syncope or presyncope in whom bradycardia or tachycardia is suspected. Ambulatory monitoring may also be indicated in patients with pacemakers, in whom pacemaker malfunction is suspected, for risk assessment post myocardial infarction, for follow up of drug therapy for arrhythmias.”

- “Requests for ambulatory monitoring should be made after careful consultation by clinicians experienced in the interpretation of rhythm disorders. It is inappropriate to request ambulatory electrocardiographic monitoring prior to careful evaluation by a clinician experienced in the pitfalls and benefits of such monitoring.”

- “Patients with suspected myocardial ischemia are generally better assessed by some sort of graduated stress evaluation, rather than by analysis of the ambulatory electrocardiogram, since it is unusual to detect asymptomatic (silent) ischemia during an ambulatory monitor in patients without stress induced ischemia. Nevertheless, ambulatory monitoring may be useful in assessing the frequency and severity of episodes of silent ischemia. Heart rate variability analysis remains highly subjective, and its role in clinical practice is very limited at present.”(46)

The ACC/AHA clinical competence statement (2001) on ECG and AECG specifies that “there are no specific guidelines that distinguish patients for whom it is appropriate to perform continuous monitoring from those for whom intermittent ambulatory monitoring is adequate”.(47) This is no longer true, as the more recent ACC/AHA/ESC 2006 ventricular arrhythmia guidelines cited earlier do make a distinction between indications for continuous 24-48 h Holter monitoring and intermittent monitoring with event

recorders. The 2004 British Columbia guidelines make the same distinction. However, no guidelines make any mention of real-time continuous attended monitoring or how indications might differ between this technology and intermittent event recorders.(41)

The clinical competence statement suggests that the frequency of symptoms should guide physician decisions about which type of monitoring to use in a particular patient. For patients with infrequent symptoms, the document suggests that intermittent event recorders may be more cost-effective. Continuous recordings are recommended for patients with daily symptoms that may be related to a heart rhythm disturbance, for patients with syncope or near syncope, and for patients with recurrent unexplained palpitations. Per the committee, continuous monitoring is also indicated in the following situations: patients receiving antiarrythmic therapy to assess drug response, to monitor the rate of atrial fibrillation, and to exclude proarrythmia; for patients with pacemakers or implantable cardioverter defibrillators (ICDs); to assess the device for myopotential inhibition and pacemaker mediated tachycardia; to assist in the optimization of physiologic programming; to evaluate if a pacemaker or ICD stopped functioning; and to assess concomitant drug therapy. Finally, continuous monitoring may be useful in assessing silent ischemia and monitoring anti-ischemia therapy.

The committee notes that, in some cases, continuous recording followed by intermittent event monitoring may be beneficial, but does not provide specific examples of this application. It also explains that while both monitoring methods are safe, AECG is problematic if it results in a delay in hospitalization or treatment. Specifically, AECG is contraindicated in patients with palpitations or altered consciousness whose etiology has been identified by history, physical examination or laboratory testing; and as an initial screening tool for ischemia if the patient is able to undergo an exercise test or for screening patients without symptoms.

B. Other Indicators

Our searches identified no evidence that indicators other than patient characteristics are used as determinants of patient eligibility for remote cardiac monitoring.

Subsection Summary

Patient eligibility for remote cardiac monitoring is determined primarily by considering patient characteristics, mostly sporadic symptoms (such as syncope, palpitations, or dizziness) suspected to be caused by arrhythmias.

Three recent guidelines propose separate indications for continuous Holter monitoring and intermittent event monitoring (with external or implanted devices). A 2006 ACC/AHA/ESC guideline on management of patients with ventricular arrhythmias states that continuous 24-48 hour Holter recordings are deemed appropriate when arrhythmias are known or suspected to occur at least once a day. Because intermittent event monitors can record over longer time periods, they are considered more appropriate when sporadic episodes produce symptoms of syncope, dizziness, or palpitations. The document does not provide clear indications for when external versus implantable event monitors should be used, although it suggests implantable recorders are useful in patients with sporadic symptoms suspected to be arrhythmia-related in whom a symptom-rhythm correlation has not been established by conventional diagnostic techniques. This guideline makes no mention of remote continuous attended monitoring systems.

A 2004 British Columbia Health Services guideline on ambulatory ECG monitoring similarly suggests that patients with daily or almost daily symptoms or those with syncope without warning may be evaluated with a 24-hour Holter monitor. Patients with less frequent symptoms may be better evaluated using a patient-activated event recorder (automatic recorders are not mentioned, nor are remote continuous attended monitoring systems).

A 2004 European Society of Cardiology guideline on management of syncope also suggests Holter monitoring as the initial strategy in patients with clinical or ECG features

of arrhythmic syncope and very frequent syncopes or presyncopes (Class I indication). Unlike other guidelines, this one states that an ILR is indicated if the mechanism of syncope remains unclear after Holter monitoring in patients with very frequent episodes of syncope (Class I indication). In patients with features of arrhythmic syncope occurring at intervals ≤4 weeks, an ELR may be used (Class II indication). An ILR may be indicated to assess the contribution of bradycardia before implanting a pacemaker in patients with suspected or certain neurally-mediated forms of syncope with frequent or traumatic syncopal episodes (Class II indication). An ILR may also be indicated in the initial phase of the work-up instead of conventional investigations in patients with preserved cardiac function who have features suggesting an arrhythmic syncope (Class II indication).

A 2006 AHA/ACCF Scientific Statement on the evaluation of syncope suggests that AECG is appropriate in patients with syncope who have had a “normal” evaluation (no underlying heart disease detected) and the diagnosis remains uncertain. The document states that a Holter monitor is appropriate for episodes that occur at least every day, and event monitoring is ideal for episodes that occur at least once a month. An ILR is considered the most likely technology to identify the mechanism of syncope in patients with unexplained syncope.

An ACC/AHA clinical competence statement suggests that the frequency of symptoms should dictate the type of recording, with intermittent recorders favored in patients with infrequent symptoms and continuous recorders favored in patients with frequent symptoms (once a day), syncope, or recurrent unexplained palpitations, among other indications.

Key Question 3: Is Management Changed Based on Information Obtained from Remote Cardiac Monitoring Using Any of the Identified Categories of Devices and Do These Changes Lead to Improvements in the Following Outcomes in Ambulatory Patients (or a Subgroup of Ambulatory Patients)?

Management change and symptom improvement due to remote cardiac monitoring devices must be considered in the context of how often these outcomes occur with conventional tests. Thus, optimal studies would directly compare remote cardiac monitoring devices to conventional approaches. Symptoms frequently investigated in the literature include unexplained syncope, presyncope, and palpitations. Conventional tests for these symptoms include 24 to 48 hour Holter monitoring; tilt table testing is often performed in patients with syncope. If one or both of these tests do not diagnose the patient's condition, this is usually when a longer-term remote monitoring strategy (>48 hours) is considered. At this point, some patients may undergo invasive electrophysiological testing, which various investigators have proposed before or after a longer-term remote monitoring strategy is initiated.

For the purposes of this question, we analyzed case series if patients had been evaluated with either Holter monitoring or (in patients with syncope) tilt table testing (or both). Additional tests such as electrophysiological testing were allowed prior to remote monitoring. However, if studies reported that patients underwent remote cardiac monitoring without previous Holter monitoring or tilt table tests, they were not included in the analyses for this question.

Evidence Base

Excluded studies: studies and the reason(s) for exclusion appear in Table D-1, Appendix D.

Discussed but not analyzed studies : Three studies and two meeting abstracts addressed this question but did not meet our criteria for analysis.(48-52) These studies appear in Tables E-1 through E-3 but are not included in the analysis for this question. Two of the three studies did not assess patients with conventional tests prior to performing remote monitoring. It is not possible to determine if arrhythmias diagnosed with remote monitoring in these studies could have also been diagnosed with conventional testing. Since remote monitoring devices are generally reserved for patients who remain undiagnosed following conventional tests, the patients in these studies may not be representative of the target population for these devices. In the third study, most patients had not been evaluataed by conventional testings. Although some patients did have prior Holter monitoring, the study did not provide separate outcome information for these patients.

Discussed and analyzed studies: Our searches identified 17 studies that addressed this question and met our criteria for analysis (see Table 5 below). Details of these studies are presented in Tables E-1 through E-3, Appendix E. Fourteen studies evaluated performance of ILRs, four studies evaluated performance of an ELR, one study evaluated a post-event recorder, and one study evaluated a real-time continuous attended monitoring device (this number adds up to 20 because three studies evaluated more than one device, see explanation below). Only one randomized trial had a parallel control group of patients undergoing conventional assessment; another trial randomized the order of monitoring strategies (all patients eventually crossed over to the other monitoring strategy by trial's end). In three other randomized trials that compared different remote monitoring devices, we evaluated each arm separately for the purposes of this question. Thus, the separate arms of these three trials were evaluated as case series (the three RCTs are also evaluated as controlled trials in Key Question 4, which addresses comparison of different devices) to include as much evidence as possible to address this question. The remaining studies were uncontrolled case series. Although controlled trials (preferably randomized) are the ideal design for assessing these devices, the case series that met our inclusion criteria selected patients who had prior Holter monitoring that had failed to diagnose their condition. Thus, management changes were unlikely without the use of a remote monitoring device.

Table 5. Evidence Base for Key Question 3

Monitor type	Study Design	References
ILR compared to "conventional" assessment	RCT	Farwell et al. 2006(10)
ILR	Before-after studies (Case series)	Giada et al. 2007(53); Brignole et al. 2006(54); Deharo et al. 2006(55); Inamdar et al. 2006(9); Brignole et al. 2005(56); Lombardi et al. 2005(57); Krahn et al. 2004(58); Armstrong et al. 2003(59); Ermis et al. 2003(60); Krahn et al. 2001(61); Krahn et al. 2001(62)[a]; Nierop et al. 2000(63); Krahn et al. 1998(64)
ELR	Before-after studies (Case series)	Brignole et al. 2006(54); Jabaudon et al. 2004(65); Rothman et al. 2007(11)[a]; Krahn et al. 2001(61)[a]
Post-event recorder	Randomized crossover trial	Kinlay et al. 1996(12)
Real-time continuous attended (MCOT)	RCT	Rothman et al. 2007(11)

[a] These studies were RCTs from which we used single-arm data for the purposes of Key Question 3

ELR – external loop recorder
ILR – implantable loop recorder
MCOT – mobile cardiac outpatient telemetry
RCT – randomized controlled trial

Quality of Included Studies

The results of our analysis of the quality of these studies are summarized in Table 6. We based the quality ratings for these studies on the criteria and information presented in Tables E-3 through Table E-6 of Appendix E. As noted in Appendix B (Strength of Evidence System), lack of a control group was considered enough of a limitation that uncontrolled case series could not score higher than moderate quality. Studies evaluating ILRs had a median quality score of 7.5 (Moderate quality) with a range from 5.0 to 9.1. The four studies that evaluated an ELR had a median quality score of 8.2 (Moderate quality, range 6.8 to 9.1), while the single study that evaluated post-event recorders was of low quality. The study evaluating remote continuous attended monitoring was of high quality.

Table 6. Quality of Included Studies Addressing Key Question 3

Reference	Year	ECRI Quality Score (Rating)
Studies evaluating ILR		
Giada et al.(53)	2007	8.2 (Moderate)
Brignole et al.(54)	2006	6.4 (Low)
Farwell et al.(10)	2006	8.5 (High)
Deharo et al.(55)	2006	7.5 (Moderate)
Inamdar et al.(9)	2006	5.0 (Low)
Brignole et al.(56)	2005	7.5 (Moderate)
Lombardi et al.(57)	2004	7.0 (Low)
Krahn et al.(58)	2004	7.0 (Low)
Armstrong et al.(59)	2003	5.9 (Low)
Ermis et al.(60)	2003	6.8 (Low)
Krahn et al.(62)	2001	7.5 (Moderate)
Krahn et al.(61)	2001	9.1 (Moderate)
Nierop et al.(63)	2000	8.4 (Moderate)
Krahn et al.(64)	1998	8.4 (Moderate)
Median quality score for ILR studies		7.5 (Moderate)

Reference	Year	ECRI Quality Score (Rating)
Studies evaluating ELR		
Giada et al.(53)	2007	8.2 (Moderate)
Rothman et al.(11)	2007	8.2 (Moderate)
Jabaudon et al.(65)	2004	6.8 (Low)
Krahn et al.(61)	2001	9.1 (Moderate)
Studies evaluating post-event recorders		
Kinlay et al.(12)	1996	6.6 (Low)
Studies evaluating remote continuous attended monitoring (MCOT)		
Rothman et al.(11)	2007	8.8 (High)

Details of Study Enrollees and Study Generalizability

Details about the patients enrolled by these studies are presented in Table E-1 to E-2 of Appendix E. Only two studies had a specific age limit in their inclusion/exclusion criteria (Brignole et al. 2006 included only patients over 30 years of age, Armstrong et al. included only patients over 60 years of age). Eight of the 14 studies evaluating ILRs had a majority of patients of age 65 or greater. In the remaining six studies, the average patient age ranged from 51 to 64 years. In 11 of 14 ILR studies, the indication for monitoring was syncope in 100% of patients. In the remaining three ILR studies, the indications for monitoring were syncope (two studies), presyncope (one study), palpitations (one study), and unexplained falls (one study). The four studies evaluating an ELR had an average patient age of 66 years, 64 years, 55 years, and 43 years, respectively. The average age of the participants in the study evaluating the post-event monitor was 45 years, while the average age of patients in the study evaluating the Cardionet real-time continuous mobile cardiac outpatient telemetry (MCOT) was 57 years. Indications for monitoring in the ELR studies varied considerably among the three studies; indications in one study were exclusively unexplained syncope, indications in another included syncope, presyncope, or palpitations, while in the third they were prior acute stroke or transient ischemic event (TIA). The post-event monitor study included only patients with palpitations. Indications for monitoring in the MCOT study included symptoms of syncope, presyncope, or severe palpitations occurring

less than once per 24 hours.The percentage of female patients varied greatly across studies, ranging from 29% to 87%.

Findings of Included Studies

Studies evaluating Insertable Loop Recorders (ILRs)

Change in Disease Management

Twelve studies with a total of 762 patients reported information on changes in disease management following implantation of ILRs (Reveal® or Reveal® Plus) in patients with suspected cardiac arrhythmias based on symptoms of syncope or presyncope. Ideally, studies addressing this question should compare ILR performance directly to performance of conventional arrhythmia assessment (usually involving a Holter monitor and/or tilt table test). Only one of these studies (Farwell et al.) was an RCT comparing ILR to conventional assessment (although the authors did not describe specifically what they meant by conventional assessment).

We used a best-evidence approach to synthesize the data from the RCT and ten additional studies, nine of which were uncontrolled case series without a comparison group (the remaining study was the ILR arm of an RCT comparing ILR to ELR). All of the uncontrolled case series reported that patients had been evaluated with Holter monitoring and/or tilt table testing without a successful diagnosis prior to receiving an ILR; this suggests that the patients were unlikely to be diagnosed without a longer-term monitoring strategy.

Individual study findings appear in Table E-7, Appendix E. This table shows both the number of patients diagnosed and the number of patients with ECG-guided treatment changes (reported separately because not all diagnosed patients required a change in treatment). Since improvement in clinical outcomes is expected primarily in patients with an actual change in treatment, we consider the latter measure to be more important than merely reporting the number of patients diagnosed.

We next determined whether the results of these studies could be synthesized to enable a conclusion regarding the direction of effect. In the ten case series, this would require imputation of a control group with an assumed rate of improvement. The RCT by Farwell et al. had a median followup of 17 months for both the ILR and conventional group; during that time, 7.1% of patients in the conventional group were diagnosed and underwent changes in treatment. We decided to use this rate as the assumed rate of improvement in the control groups for the other ten studies. Since most of the other studies had shorter mean or median follow-up periods (the shortest being seven months), this is a conservative estimate. It also serves as a starting point for further sensitivity analyses.

One study was not included in the synthesis because it was a study of patients diagnosed with vasovagal syncope after tilt table testing; ILR was used to look for a symptom-rhythm correlation and to help determine the appropriate treatment.
By contrast, all of the other studies evaluated ILR in patients who had remained undiagnosed after Holter and/or tilt table testing.

An additional ILR study with 26 patients was not included in the synthesis because the patients had experienced palpitations, whereas all patients in the other studies had experienced syncope or presyncope. Patients with palpitations may not be comparable to patients experiencing syncope, and the utility of ILR monitoring could differ among these subgroups of patients. This was a single moderate-quality study that by itself had insufficient evidence for a conclusion.

The findings of the synthesis are summarized in Figure 3. We did not perform heterogeneity testing because of the imputation described above. Further, it is inappropriate to perform a meta-analysis for the purpose of providing a quantitative estimate of the between-group difference in effectiveness. We therefore conducted a series of sensitivity analyses for the purpose of reaching a qualitative conclusion about the direction of effect. The results indicate that a significantly larger number of patients with unexplained syncope undergo changes in disease management with ILR monitoring than with conventional arrhythmia assessment. Multiple sensitivity analyses

(including removal of each study separately, cumulative meta-analysis by publication date, and increasing the control group change in management rate to 20%) supported the robustness of this conclusion (seeTable E-11, Appendix E). The median quality of these studies is moderate (median 7.5, range 5.0 to 8.4; see Table E-3 and Table E-4, Appendix E for more details) and the findings are robust. Therefore, the strength of evidence supporting this conclusion is moderate.

Table 7. ILR – Change in Management

Study	Number of patients (N)		% patients with ECG-guided treatment changes (n/N)	
Farwell et al. 2006(10)	103	Control: 98	41.7 (43/103)	Control: 7.1 (7/98)
Inamdar et al. 2006(9)	100		45 (45/100)	
Brignole et al. 2005(56)	103		36.9 (38/103)	
Lombardi et al. 2005(57)	34		32.4 (11/34)	
Krahn et al. 2004(58)	60		35 (21/60)	
Armstrong et al. 2003(59)	15		20 (3/15)	
Ermis et al. 2003(60)	50		32 (16/50)	
Krahn et al. 2001(62)	85		15.3 (13/85)	
Krahn et al. 2001(61)	30		46.7 (14/30)	
Nierop et al. 2000(63)	35		22.9 (8/35)	
Krahn et al. 1998(64)	24		75 (18/24)	

Syncopal Episodes

Four studies (one RCT, two case series, and a single arm from another RCT) with a total of 369 patients reported syncopal episodes following ILR implantation, although this was reported using different methods of measurement (Table E-8, Appendix E).
In an RCT with 201 patients, Farwell et al. reported the total percentage of patients with recurrent syncope, the percentage of patients with a second recurrence of syncope, and the time to second syncope recurrence. The first two measures showed no significant difference between ILR and conventional assessment, while time to second syncope recurrence showed a statistically significant difference favoring ILR ($p = 0.04$). This

study also reported time to first syncope recurrence, but this is not a useful measure because no patients were diagnosed until at least the first syncope recurrence. Without a change in disease management (which would not occur until diagnosis), a reduction in syncope recurrence would not be expected for most patients (syncope can resolve without treatment in some patients, but the proportion should be similar in both arms of the trial).

The study by Brignole et al. began as a case series, but in Phase II they separated patients diagnosed by ILR into two groups: one group of 53 patients received ILR-based specific therapy, while the other group of 50 patients received no specific therapy. During a median followup of nine months, the group with ILR-based specific therapy had a significantly lower syncope recurrence rate compared to the non-specific therapy group (11% vs 34%, $p = 0.008$).

Two additional studies lacked a parallel control group. The study by Krahn et al. reported only the number of diagnosed patients with syncope resolution; they did not report the number of undiagnosed patients with syncope resolution, which would be required for an accurate assessment of ILR monitoring (since syncope can resolve without treatment). The case series by Nierop et al. compared the mean syncope rate in patients for one year before ILR implant and one year after ILR implant. Although they found a statistically significant reduction in mean syncope rate one year after ILR implant ($p < 0.01$), they only compared these numbers in 50% of the patients (the only patients who had at least one year of followup). Furthermore, a parallel control group would be required to confirm that the observed decrease was not simply due to regression to the mean (i.e., symptoms may have spontaneously regressed after peaking).

These studies varied in quality (the RCT high, two moderate, one low), and the findings were not combined because of the different measures and different comparisons used in each study. The only high-quality study with a parallel control group found an increase in the time to second syncope but no statistically significant decrease in the recurrence rate. However, the providers were not blinded and received manufacturer

funding, and the between-groups difference in time to recurrence (p = 0.04) was not large enough to allow a conclusion based on one single-center study. These findings differed somewhat from the low-quality comparative trial, which found a statistically significant reduction in syncope recurrence associated with ILR monitoring. However, this study was not randomized or blinded and showed evidence of selection bias (patients with asystole were predominantly selected for the specific therapy group). In addition, the comparison differs somewhat from the comparison in the RCT (which was based on syncope recurrence among any patients in the two arms, not just among diagnosed patients). Because of these differences, and because the two other studies lacked essential comparative data, the evidence is insufficient to allow a conclusion regarding the effect of ILR implantation (with associated ILR-guided treatment changes) on syncopal episodes.

Mortality

Three studies (one RCT, two case series) with a total of 389 patients with at least one year of followup reported mortality after ILR implantation (Table E-9, Appendix E). The RCT found no significant difference in mortality rates between ILR and conventional assessment over a median followup of 17 months. Although the two case series reported mortality among ILR patients during a similar follow-up period, an analysis of mortality in uncontrolled case series would require that mortality in diagnosed patients be compared to mortality in undiagnosed patients. Otherwise, one cannot determine whether the deaths occurred in patients who had not been diagnosed or whose treatment was not changed (and therefore might be expected to have worse outcomes). Thus, the case series data are insufficient for an analysis of mortality, and the results of the RCT are inconclusive (because the 95% CI around the summary effect was too wide to rule out a difference between treatments).

Quality of life

The RCT by Farwell et al. was the only study to report quality-of-life data, measured using the SF-12 questionnaire and a visual analogue scale (VAS) for general well-being (Table E-10, Appendix E). At 6, 12, and 18 months followup, no changes were observed in the SF-12 questionnaire in the ILR group compared to the conventional assessment

group. For the VAS, no between-group differences were observed at 6 and 12 months, but a significant between group difference (p = 0.03) favoring ILR was observed at 18 months. However, the authors note the difficulty in measuring quality of life in a syncopal population because of the “rare and random nature of the symptom”.(10) Furthermore, this is a single-center study with no blinding of providers, the evidence on quality of life is inconsistent (results differ for different quality-of-life instruments), and the one statistically significant difference is not a large effect. Therefore, the evidence is insufficient to allow a conclusion regarding the effect of ILR monitoring on quality of life.

Other outcomes

One study reported data on palpitations that could not be interpreted due to lack of adequate comparative data. No studies meeting our inclusion criteria reported data on the following outcomes: TIAs and non-fatal stroke, dyspnea or heart failure, and angina or MI.

Studies evaluating External Loop Recorders (ELRs)

Change in Disease Management

Four studies with 318 patients reported change in disease management in patients after monitoring with an ELR (enrollment criteria and patient characteristics appear in Tables E-1 and E-2, Appendix E). None of these studies included a parallel control group of patients who were only evaluated using conventional assessment. Three of these studies were taken from the ELR arm of RCTs that compared ELR to other remote monitoring devices. However, the indications for monitoring differ considerably among these studies. One study evaluated only patients with unexplained syncope, another study combined patients with syncope, presyncope, and palpitations, another study evaluated only patients with palpitations, and the remaining study used ELRs to monitor patients after a stroke or transient ischemic attack (TIA) for the occurrence of atrial fibrillation or atrial flutter. These differences in the patient selection criteria for each study create clinical heterogeneity that precludes combining the data from these studies. Even if one assumes that additional conventional tests (e.g., tilt table) would not have led to a change in management for any patients in these studies, only one of the

four studies showed a large effect (Rothman et al. with 14.6% of patients whose management was changed due to ELR [Table E-7, Appendix E]), and only if one assumes that the rate would have been close to zero in a hypothetical control group. Given the low-to-moderate quality of these studies (Table E-5, Appendix E) and the lack of data for estimating a control group change in management rate, the evidence is insufficient to determine whether ELR monitoring can lead to a change in disease management in patients who have already undergone conventional assessment.

Syncopal Episodes

One RCT comparing ELR to ILR reported resolution of syncope among diagnosed patients; for this question, we considered only the patients who were monitored with an ELR device (6/6 diagnosed patients had resolution of syncope). Only four of these patients had an actual management change made following diagnosis, and the authors did not report the number of undiagnosed patients who had resolution of syncope. Thus, the evidence is insufficient to determine whether ELR is associated with a reduction in syncopal episodes.

Other Outcomes

One study reported data on palpitations that could not be interpreted due to lack of adequate comparative data. No study of ELR that met our inclusion criteria reported any other outcomes of interest.

Studies Evaluating Post-Event Recorders

Change in Disease Management

One randomized crossover trial with 45 patients with palpitations reported change in disease management after monitoring with a post-event recorder (enrollment criteria and patient characteristics appear in Tables E-1 and E-2, Appendix E). After a mean followup of three months, eight out of 45 patients underwent a change in management based on detection of a clinically significant arrhythmia by the post-event recorder. None of these events was detected when the same patients were monitored by a Holter monitor (Table E-7, Appendix E). However, this “conventional” assessment period

(two days) was much shorter than the period of time allotted for post-event recorder monitoring (three months). In that sense, this trial is very similar to case series of patients who had non-diagnostic Holter monitoring prior to a longer-duration remote monitoring technology. Therefore, this study's quality was scored using the quality scale for before-after studies. Because this was a single small study of moderate quality (lack of consecutive patient enrollment, susceptibility of outcome to biased interpretation, funding source not reported; see Table E-5, Appendix E), the evidence is insufficient to allow a conclusion for this outcome.

Other Outcomes

This study did not report any other outcomes of interest.

Studies Evaluating Real-Time Continuous Attended Remote Cardiac Monitoring Devices

Change in Disease Management

One study with 266 patients reported change in disease management in patients after monitoring with an MCOT System (enrollment criteria and patient characteristics appear in Tables E-1 and E-2, Appendix E). This was a multicenter RCT that compared MCOT and ELRs, a comparison addressed in Key Question 4. For the purposes of this question, however, one can assume that the rate of change in disease management observed in the ELR arm was not lower than the rate that would have been observed with continued conventional assessment. Study results appear in Table E-7, Appendix E. In this study, MCOT detected clinically significant arrhythmias (requiring treatment) in a substantially larger number of patients (55/134, 41%) over a 25-day monitoring period compared to ELR (19/132, 14.4%), a roughly three-fold difference that was statistically significant ($p < 0.001$). This is a high-quality multicenter study with few limitations; although investigators were not blinded, outcome assessors (those reading the EKG data) were blinded, which decreases the chance of biased interpretation. Although compliance was difficult to monitor in the ELR group, the percentage of dropouts due to non-compliance was low in both groups. Thus, the evidence is sufficient to conclude

that MCOT real-time monitoring leads to a change in disease management in significantly more patients than does conventional assessment. Because this is a single multicenter study, the strength of evidence supporting this conclusion is weak.

Other Outcomes

The study that met our inclusion criteria for this question did not report data on any other relevant outcomes.

Subsection Summary

Patients with unexplained syncope are more likely to undergo a change in disease management when using ILR monitoring or real-time continuous attended monitoring than conventional assessment (i.e., Holter monitoring and/or tilt table testing). Patients with severe palpitations occurring less than once per 24 hours are also more likely to undergo a change in disease management when using real-time continuous attended monitoring. The strength of evidence is moderate for ILR (based on 11 studies, average quality moderate), and weak for real-time continuous monitoring (based on one high-quality multicenter trial). Due to small numbers of studies identified and numerous quality flaws, the evidence is insufficient to evaluate the effect of other remote monitoring devices (ELRs and post-event recorders) on change in disease management. For the same reasons, the evidence is insufficient to determine whether any class of remote cardiac monitoring devices are associated with better clinical outcomes than conventional monitoring.

Key Question 4: Of the Patient Outcomes for which Improvements Have Been Demonstrated, Do Any Categories of Devices (As Listed Under Question 1) Lead to Greater Improvement in These Outcomes in Ambulatory Patients (or a Subgroup of Ambulatory Patients) Compared to Any of the Other Categories of Devices?

Evidence Base

Our searches identified three RCTs with 376 patients that addressed this question (see Table 8 below). Two studies with 110 patients compared a prolonged monitoring strategy with ILR to a strategy involving use of ELR plus other tests (tilt table testing and/or electrophysiological testing) for assessment of unexplained syncope (one study) or palpitations (one study). The remaining study (266 patients) compared real-time continuous attended monitoring (with the MCOT system) to ELR monitoring.

Table 8. Evidence Base for Key Question 4

Device comparison	Study Design	References
ILR vs ELR + electrophysiological testing	Randomized controlled trial	Giada et al. 2007(53)
ILR vs ELR + tilt table + electrophysiological testing	Randomized controlled trial	Krahn et al. 2001(61)
MCOT vs ELR	Randomized controlled trial	Rothman et al. 2007(11)

Quality of Included Studies

The studies by Giada et al. and Krahn et al. were of moderate quality, while the study by Rothman et al. was of high quality (for further details see Table F-3, Appendix F).

Details of Study Enrollees and Study Generalizability

Study enrollment criteria and patient characteristics appear in Tables F-1 and F-2, Appendix F). The majority of patients in the trial by Giada et al. were in their 40s, 67% were women, and the indication for monitoring in all patients was palpitations. In contrast, the majority of patients in the trial by Krahn et al. were age 65 or older,

45% were women, and all of the patients in this study were monitored for syncope. In the trial comparing MCOT and ELR, the majority of patients were below age 65 (average 56) and approximately 65% were women. Indications for monitoring in this study included syncope, presyncope, and severe palpitations occurring less than once per 24 hours.

Findings of Included Studies

Change in Disease Management

In the single-center study comparing ILR to ELR plus other tests in patients with syncope (60 patients total), Krahn et al. reported that 46.7% of ILR patients and 3.3% of ELR patients underwent a change in disease management as a result of remote monitoring (Table F-4, Appendix F). This difference was statistically significant ($p = 0.0002$). The ELR percentage does not include five patients who were diagnosed by tilt table or electrophysiological testing following ELR monitoring. Patients in the ILR group received pacemakers, antiarrhythmic drugs, or dietary interventions, while the ELR patient received a pacemaker. The single-center study of Giada et al. showed similar qualitative findings in 50 patients with palpitations. Giada et al. reported that 73% of ILR patients and 8.3% of ELR patients underwent a change in disease management as a result of remote monitoring (Table F-4, Appendix F). This difference was statistically significant ($p = 0.0001$). The ELR percentage does not include three patients who were diagnosed by electrophysiological testing following ELR monitoring.

These studies had several limitations. In both studies, the length of followup differed significantly between the two groups. ILR patients were followed for up to one year, while ELR patients were followed for two to five weeks on average. This is mostly reflective of the nature of these technologies, and as such may be reflective of clinical practice. Any ELR patients undiagnosed after one month were allowed to cross over to ILR monitoring. Thus, the percent of patients who might have been diagnosed during a year of followup in the ELR arm without crossover to ILR is unknown (although an ELR is generally not worn this long, intermittent conventional assessment is possible during followup). In addition, investigators and outcome assessors were not blinded, allowing potential bias that might affect the trial results. These and other limitations, including

between-group differences in baseline patient characteristics (Table F-3, Appendix F), indicate that these two small, single-center studies are of moderate quality. Furthermore, the two studies each evaluated clinically different patient populations (patients with palpitations in their 40s vs patients with syncope and age 65 or older), which precluded combining the data in a meta-analysis. Therefore, the evidence is insufficient to allow a conclusion regarding change in management in patients with unexplained syncope or palpitations monitored with ILR vs ELR.

In the multicenter study comparing MCOT to ELR (266 patients total), Rothman et al. reported that a substantially larger number of patients had detection of a clinically significant arrhythmia (requiring management change) in the MCOT-monitored group (55/134 patients, 41%) compared to the ELR-monitored group (19/132 patients, 14.4%), a roughly three-fold difference that was statistically significant (Table F-4, Appendix F). In the subgroup of patients with syncope/presyncope, the respective percentages were 51.6% for MCOT and 15.7% for ELR. This is a high-quality multicenter study with few limitations; although investigators were not blinded, outcome assessors (those reading the EKG data) were blinded, which decreases the chance of biased interpretation. Although compliance was difficult to monitor in the ELR group, the percentage of dropouts due to non-compliance was low in both groups. This evidence is sufficient to conclude that MCOT leads to change in disease management in significantly more patients than do certain ELRs. Because this is a single multicenter study, the strength of evidence supporting this conclusion is weak.

Most patients received patient-activated ELRs, while some patients (at two out of 15 sites) received auto-trigger ELRs. This latter type of ELR is more similar in mechanism to the MCOT device (which has automatic event activation). The authors performed a subgroup analysis of auto-trigger ELRs; although the findings did not differ from the main study results, this was a post hoc analysis (not pre-planned at study initiation) and thus cannot be considered sufficient evidence for a conclusion about this subgroup of ELRs. Furthermore, only 16% of patients used auto-trigger ELRs. In short, the overall conclusion should not be generalized to this type of ELR pending further study.

Reduction in Syncope

Krahn et al. reported that 27 of 29 patients diagnosed during followup with either ILR or ELR plus tilt table plus electrophysiological testing had complete resolution of syncope. Based on their description, we were able to determine that 20 patients had resolution of syncope following ILR-guided treatment changes, while seven patients had resolution of syncope following ELR-based treatment changes. Of the patients with ILR-guided treatment changes, 13 received ILR as the primary intervention and seven received ILR after crossover from the ELR group (patients who were not diagnosed by the primary intervention after a certain period were allowed to crossover to receive the alternative intervention). Of the patients with ELR-guided treatment changes, six received ELR as the primary intervention and one crossed over from the ILR group. Since only some of the patients undiagnosed by the primary intervention crossed over to the alternative intervention, an analysis of syncope resolution should focus only on patients who did not cross-over to another intervention. The authors did not report the number of undiagnosed patients who experienced resolution of syncope during followup. The major flaw of this outcome comparison is that most patients undiagnosed after one month of ELR monitoring crossed over to ILR monitoring. Therefore, it is impossible to determine what percentage of these patients might have had resolution of syncope after a year without ILR monitoring. This is problematic because syncope can resolve spontaneously without treatment in some patients. An accurate comparison would require an equal followup in both groups without crossover to another monitoring strategy. Therefore, the lack of an adequate control group means that the evidence is insufficient to allow a conclusion for this outcome.

Other Outcomes

Neither study reported any other relevant outcomes.

Subsection Summary

Three RCTs with 376 patients addressed this question. Two studies compared a prolonged monitoring strategy with ILR to a strategy involving use of ELR plus other tests (tilt table testing and/or electrophysiological testing) for assessment of unexplained syncope (one study) or palpitations (one study). These studies found a statistically significant increase in the proportion of patients whose management was changed in the ILR group. However, these studies had several limitations, including baseline differences in patient characteristics and lack of blinding of outcome assessors. Furthermore, the two studies each evaluated clinically different patient populations (patients with palpitations vs patients with syncope), which precluded combining the data in a meta-analysis. Therefore, the evidence is insufficient to allow a conclusion about the relative benefits of ILRs and ELRs in patients with unexplained syncope or palpitations.

The other RCT compared MCOT and ELR, and found that a substantially larger number of patients had detection of clinically significant arrhythmias (requiring management change) in the MCOT group (55/134 patients, 41.4%) compared to the ELR group (19/132 patients, 14.6%). The difference was statistically significant (difference between groups $p < 0.001$). Most participating centers used patient-activated ELRs, while two of the centers used ELRs with automatic event activation. This study was a high-quality multicenter study with few limitations. Therefore, the evidence is sufficient to conclude that MCOT leads to change in disease management in significantly more patients than do certain ELRs. Because this is a single multicenter study, the strength of evidence supporting this conclusion is weak. Also, the conclusion may not be applicable to ELRs with automatic event activation, as this model was underrepresented in the RCT.

One study comparing ILR monitoring to ELR monitoring evaluated a patient-oriented outcome (reduction in syncope). However, because the comparison was inadequately controlled in this single study, the evidence was insufficient to allow a conclusion for this outcome. No other patient-oriented outcomes were evaluated by any studies in this evidence base.

Key Question 5: Of the Patient Outcomes for which Improvements Have Been Demonstrated, Do Any Devices within a Category Lead to Greater Improvement in These Outcomes in Ambulatory Patients (or a Subgroup of Ambulatory Patients) Compared to Any of the Other Devices within the Same Category?

Evidence Base

Our searches identified no studies that addressed this question.

Key Question 6: What Accreditation Standards Exist for Training and Continuing Education for the Interpretation of Data from Remote Cardiac Monitoring?

Our searches identified two relevant documents for practices in the United States, one dealing specifically with training for ambulatory electrocardiography (AECG) and another for credentialing. In addition, one non-U.S. training-related reference was identified.

Training Within the United States

The American College of Cardiology (ACC)/ American Heart Association's (AHA) Clinical Competence Statement on Electrocardiography and Ambulatory Electrocardiography (2001) describes the minimum education, training, experience and cognitive/technical skills necessary to competently interpret AECGs. Because of variation in the analysis, reporting, and recording features of existing ambulatory systems, the document addresses only the features common to all ambulatory electrocardiographic systems.(47)

As AECG is a clinical subdivision of ECG, the ACC/AHA committee expects that those interpreting AECGs will meet the criteria for competence for classic (12-lead) ECG. In addition, as there are a variety of AECGs available, the committee stresses that physicians interpreting the transmitted data must understand the equipment, the data collection process, and techniques used to perform AECGs on the specific system with

which they are working. They also recommend that physicians interpreting these recordings must be aware of the numerous sources of interference (i.e., noise, low-voltage recording, etc.) with these devices.

The ACC/AHA committee recommends supervised interpretation of a minimum of 150 AECGs be considered necessary for minimum competence. The committee states that many physicians receive this training during residency or while in a fellowship training program and accepts that some of this experience may be gained from a 'teaching set' of AECGs which range from normal to abnormal. The committee notes that this training should be documented in a logbook. The task force also suggested attending well-designed courses conducted by expert AECG readers, but stated that course attendance does not eliminate the need for supervised interpretation of a minimum of 150 AECGs.

To maintain competence, the Task Force recommends physicians complete a minimum of 25 interpretations per year and that an expert review their interpretations for quality assurance purposes.(47)

Credentialing Within the United States

Contracted Licensed Independent Practitioners (LIPs) who read and interpret data transmitted to a remote site need to be credentialed and privileged at both the distant and originating (facility receiving the telemedicine service) site. If the remote site is a Joint Commission-accredited organization, the originating site may use both the credentialing and privileging decisions from the remote site. In cases where the remote site is not Joint Commission-accredited or if the practitioner was hired directly, the originating site is responsible for credentialing and privileging that practitioner as if he/she was at the original site. There are no specific Joint Commission credentialing and privileging requirements for practitioners who do not direct patient care but instead work in a consultation capacity only (advising the treating physician) (Joint Commission Perspectives February 2003).(66)

Training Outside of the United States

The Cardiac Society of Australia and New Zealand has published a guideline with criteria for competence in AECG monitoring. They require practitioners to receive supervised postgraduate training at an institution recognized for its excellence in this area. Under the supervision of an expert physician electrocardiographer, at least 100 AECGs spanning the range from abnormal to normal should be read and interpreted by the postgraduate student.(46)

Subsection Summary

Standards for training in AECG generally expect trainees to meet the same competence criteria required for interpretation of classic 12-lead ECG. ACC/AHA recommends supervised interpretation of a minimum of 150 AECGs be considered necessary for minimum competence. To maintain competence, ACC/AHA recommends physicians complete a minimum of 25 interpretations per year and that an expert review their interpretations for quality assurance purposes. A guideline from the Cardiac Society of Australia and New Zealand recommends that at least 100 AECGs spanning the range from abnormal to normal should be read and interpreted by a supervised postgraduate student.

Credentialing criteria in the U.S. are addressed by a Joint Commission document that states that Contracted Licensed Independent Practitioners (LIPs) who read and interpret data transmitted to a remote site need to be credentialed and privileged at both the distant and originating (facility receiving the telemedicine service) site. If the remote site is a Joint Commission-accredited organization, the prescribing site may use both the credentialing and privileging decisions from the remote site. In cases where the remote site is not Joint Commission-accredited or if the practitioner was hired directly, the originating site is responsible for credentialing and privileging that practitioner as if he/she was at the original site.

Key Question 7: What Standards Exist to Guide How Data Gathered from Remote Cardiac Monitors Should Be Incorporated into a Patient's Continuum of Care? In Practice (i.e., as Reported in the Published Literature, "Gray Literature", etc.), What Are the Characteristics of the Patient Care Infrastructure Using Remote Cardiac Monitoring (e.g., Use of Either Attending Technicians or Attending Physicians) and How Are the Data Gathered from Remote Cardiac Monitoring Used to Inform Patients' Continuum of Care?

Our searches identified no formal standards that addressed this question. However, information regarding the patient care infrastructure for remote cardiac monitoring systems is available from manufacturer Web sites, FDA documents and published articles. Information relevant to this question was obtained primarily from the first two sources; studies that addressed Key Questions 3 and 4 did not provide any additional information on infrastructure that was not reported by these other sources. Important issues in patient care infrastructure include methods of data collection, whether monitoring is attended or unattended, who collects and analyzes the data, what is the patient care protocol, and what information becomes part of the medical record.

The patient care infrastructure for real-time continuous attended cardiac monitoring is very similar among the three available systems (MCOT, Heartlink II, and VST™, see Table G-1, Appendix G). Each system automatically transmits event-related ECGs to a central monitoring laboratory which collects and stores remote ECG data. These central laboratories are attended 24 hours a day, seven days a week by trained staff (centers for MCOT and Heartlink II use "certified technicians", while the center for VST™ uses nurses or critical care "specialists"). ECGs are analyzed by monitoring staff or software programs, and the patient's physician either receives daily reports or can access patient reports at any time during the monitoring period. One system (VST™) generates a summary report for the physician at the end of monitoring. Recorded events and diagnoses presumably are incorporated by the physician into a patient's medical record, although this is not clearly stated in published sources.(1,18,19)

The patient care infrastructure for patient- or event-activated loop recorders and post-event recorders is in general not well described in published documents (Table G-1, Appendix G). Some manufacturers provide fully-attended monitoring centers for their devices; we have listed such devices as attended in Table G-1 of Appendix G when the information was verifiable from manufacturer Web sites. However, any device with transtelephonic or wireless transmission has the option of fully-attended monitoring by an Independent Diagnostic Testing Facility. Given that the major CPT codes for looping recorders and post-event recorders specify 24-hour attended monitoring,(67) it is likely that attended monitoring is often used for these devices, even if this is not described by manufacturer or FDA documents. Thus, Table G-1 lists most of these devices as "optional" with regard to attended monitoring. Attended monitoring centers (usually staffed by technicians, although the type of staff was not reported for most centers) will notify the patient's physician of critical events, and some prepare daily reports for the physician. ECG data sent to a receiving center or a PC is generally available for access by the patient's physician at any time. ECG data can only be retrieved from an ILR during patient visits to a physician's office. As noted earlier, what data are incorporated into the patient's medical record from any of these devices are unclear.

A small study has suggested that remote cardiac monitoring can potentially decrease the number of referrals from general practice to cardiology clinics. Twenty-seven general practitioners used the C.Net2000, a patient-activated ELR, for remote monitoring of 73 patients with symptoms possibly related to cardiac arrhythmias. This was after an initial clinical assessment where they had identified patients who they intended to refer to cardiologists for further testing. The study found that the ELR reduced the number of patients initially intended for referral from 49 to 19 patients, a decrease of about 60%.(68) This study contrasts with most of the studies included in Key Question 3 and 4, where remote monitoring was generally used in patients who remained undiagnosed after Holter monitoring in cardiology departments or clinics.

Subsection Summary

Our searches identified no formal standards that addressed this question. However, they did identify documents that provided some information regarding patient care

infrastructure. Important issues in patient care infrastructure include methods of data collection, whether monitoring is attended or unattended, who collects and analyzes the data, what is the patient care protocol, and what information becomes part of the medical record. More of these types of information was available on devices that transmit ECG data to attended monitoring centers (which includes all of the remote continuous attended monitoring devices). Attended monitoring centers are usually staffed by technicians (occasionally other health professionals) who analyze ECG data and report critical events to a patient's physician. Some centers send daily reports and/or a final summary report to the physician, and data are generally accessible to the physician at all times. The majority of patient- or event-activated intermittent recorders (looping or post-event) at least have the option of being attended by a fully-staffed monitoring center. Patient care protocols generally are not well described for most devices. However, stored ECG data are usually accessible by physicians during the monitoring period. The information that is incorporated into medical records was not clearly described in source documents for any of these devices, although we assume that, at minimum, important events and diagnoses are entered into these records.

Conclusions

Summary for Key Question 1

Several devices are currently used to remotely assess cardiac rhythm abnormalities in ambulatory patients. These devices can be categorized according to whether they monitor cardiac rhythm intermittently or continuously, whether they are worn externally or implanted, and whether they have looping memory. Patient/event-activated intermittent recorders (pre-symptom continuous loop and post-symptom recorders) comprise the largest category of devices. Within this broad category, external loop recorders (patient- and/or event-activated) are the largest subcategory, with 31 identified devices. Real-time continuous attended remote cardiac monitoring is the newest category, with four commercially-available devices.

Summary for Key Question 2

Patient eligibility for remote cardiac monitoring is determined primarily by considering patient characteristics, mostly sporadic symptoms (such as syncope, palpitations, or dizziness) suspected to be caused by arrhythmias.

Three recent guidelines propose separate indications for continuous Holter monitoring and intermittent event monitoring (with external or implanted devices). A 2006 ACC/AHA/ESC guideline on management of patients with ventricular arrhythmias states that continuous 24-48 hour Holter recordings are deemed appropriate when arrhythmias are known or suspected to occur at least once a day. Because intermittent event monitors can record over longer time periods, they are considered more appropriate when sporadic episodes produce symptoms of syncope, dizziness, or palpitations. The document does not provide clear indications for when external versus implantable event monitors should be used, although it suggests implantable recorders are useful in patients with sporadic symptoms suspected to be arrhythmia-related in whom a symptom-rhythm correlation has not been established by conventional diagnostic techniques. This guideline makes no mention of real-time continuous attended monitoring systems.

A 2004 British Columbia Health Services guideline on ambulatory ECG monitoring similarly suggests that patients with daily or almost daily symptoms or those with syncope without warning may be evaluated with a 24-hour Holter monitor. Patients with less frequent symptoms may be better evaluated using a patient-activated event recorder (automatic recorders are not mentioned, nor are real-time continuous attended monitoring systems).

A 2004 European Society of Cardiology guideline on management of syncope also suggests Holter monitoring as the initial strategy in patients with clinical or ECG features of arrhythmic syncope and very frequent syncopes or presyncopes (Class I indication). Unlike other guidelines, this one states that an ILR is indicated if the mechanism of syncope remains unclear after Holter monitoring in patients with very frequent episodes of syncope (Class I indication). In patients with features of arrhythmic syncope occurring at intervals ≤4 weeks, an ELR may be used (Class II indication). An ILR may be

indicated to assess the contribution of bradycardia before implanting a pacemaker in patients with suspected or certain neurally-mediated forms of syncope with frequent or traumatic syncopal episodes (Class II indication). An ILR may also be indicated in the initial phase of the work-up instead of conventional investigations in patients with preserved cardiac function who have features suggesting an arrhythmic syncope (Class II indication).

A 2006 AHA/ACCF Scientific Statement on the evaluation of syncope suggests that AECG is appropriate in patients with syncope who have had a “normal” evaluation (no underlying heart disease detected) and the diagnosis remains uncertain. The document states that a Holter monitor is appropriate for episodes that occur at least every day, and event monitoring is ideal for episodes that occur at least once a month. An ILR is considered the most likely technology to identify the mechanism of syncope in patients with unexplained syncope.

An ACC/AHA clinical competence statement suggests that the frequency of symptoms should dictate the type of recording device used. For patients with infrequent symptoms, the document suggests that intermittent event recorders may be more cost-effective.

Continuous recordings are indicated for patients with frequent symptoms (at least once a day) that may be arrhythmia-related, for patients with syncope or near syncope, and for patients with recurrent unexplained palpitations. Per the committee, continuous monitoring is also indicated in the following situations: patients receiving antiarrythmic therapy to assess drug response, to monitor the rate of atrial fibrillation, and to exclude proarrythmia.

For patients with pacemakers or implantable cardioverter defibrillators (ICDs), continuous monitoring is indicated to assess the device for myopotential inhibition and pacemaker-mediated tachycardia; to assist in the optimization of physiologic programming; to evaluate if a pacemaker or ICD stopped functioning; and to assess concomitant drug therapy.

Continuous monitoring may also be useful in assessing silent ischemia and monitoring anti-ischemia therapy.

Summary for Key Question 3

This question addressed whether management is changed or outcomes improved based on information obtained from remote monitoring devices. Patients with unexplained syncope are more likely to undergo a change in disease management when using ILR monitoring or real-time continuous attended monitoring than when using conventional assessment (i.e., Holter monitoring and/or tilt table testing). Patients with severe palpitations occurring less than once per 24 hours are also more likely to undergo a change in disease management when using real-time continuous attended monitoring. The strength of evidence is moderate for ILR (based on 11 studies, average quality moderate), and weak for real-time continuous monitoring (based on one high-quality multicenter trial). Due to small numbers of studies identified and numerous quality flaws, the evidence was insufficient to evaluate the effect of other remote monitoring devices (ELRs and post-event recorders) on change in disease management. For the same reasons, the evidence was also insufficient to determine if any class of remote cardiac monitoring devices results in better clinical outcomes than conventional monitoring.

Summary for Key Question 4

Three RCTs with 376 patients addressed this question regarding superiority of any category of device. Two studies with 110 patients compared a prolonged monitoring strategy with ILR to a strategy using ELR plus other tests (tilt table testing and/or electrophysiological testing) for assessment of unexplained syncope (one study) or palpitations (one study). These studies found a statistically significant increase in the proportion of patients undergoing a change in disease management in the ILR group compared to the ELR group. However, these are small studies with several limitations (including between-group differences in baseline patient characteristics and lack of blinding of outcome assessors). Furthermore, the two studies each evaluated clinically different patient populations (patients with palpitations vs patients with syncope), which precluded combining the data in a meta-analysis. Therefore, the evidence is insufficient to allow a conclusion about the relative benefits of ILR monitoring vs ELR monitoring in patients with unexplained syncope or palpitations.

The other study (266 patients) compared real-time continuous attended monitoring (MCOT) with ELR monitoring and found that a substantially larger number of patients had detection of clinically significant arrhythmias (requiring management change) in the MCOT group (55/134 patients, 41%) compared to the ELR group (19/132 patients, 14.4%). The difference was statistically significant (difference between groups: $p < 0.001$). Most participating centers used patient-activated ELRs, while two of the centers used ELRs with automatic event activation. This study was a high-quality multicenter study with few limitations. Therefore, the evidence is sufficient to conclude that real-time continuous attended monitoring leads to change in disease management in significantly more patients than do certain ELRs. However, because this is a single multicenter study, the strength of evidence supporting this conclusion is weak. Also, the conclusion may not be applicable to ELRs with automatic event activation, as this model was underrepresented in the RCT (only 16% of patients used this model).

One study comparing ILR monitoring to ELR monitoring evaluated a patient-oriented outcome (reduction in syncope). However, because the comparison was inadequately controlled in this single study, the evidence was insufficient to allow a conclusion for this outcome. No other patient-oriented outcomes were evaluated by any studies in this evidence base.

Summary for Key Question 5

Our searches identified no studies that addressed this question.

Summary for Key Question 6

Standards for training in AECG generally expect trainees to meet the same competence criteria required for interpretation of classic 12-lead ECG. ACC/AHA recommends supervised interpretation of a minimum of 150 AECGs be considered necessary for minimum competence. To maintain competence, ACC/AHA recommends physicians complete a minimum of 25 interpretations per year and that an expert review their interpretations for quality assurance purposes. A guideline from the Cardiac Society of Australia and New Zealand recommends that at least 100 AECGs spanning the range from abnormal to normal should be read and interpreted by a supervised postgraduate student.

Credentialing criteria in the U.S. are addressed by a Joint Commission document that states that Contracted Licensed Independent Practitioners (LIPs) who read and interpret data transmitted to a remote site need to be credentialed and privileged at both the distant and originating (facility receiving the telemedicine service) site. If the remote site is a Joint Commission-accredited organization, the prescribing site may use both the credentialing and privileging decisions from the remote site. In cases where the remote site is not Joint Commission-accredited or if the practitioner was hired directly, the originating site is responsible for credentialing and privileging that practitioner as if he/she was at the original site.

Summary for Key Question 7

Our searches identified no formal standards that addressed this question. However, information regarding the patient care infrastructure for remote cardiac monitoring systems is available from manufacturer Web sites, FDA documents and published articles. Information relevant to this question was obtained primarily from manufacturer Web sites and FDA documents; studies that addressed Key Questions 3 and 4 did not provide any additional information on infrastructure that was not reported by these other sources. Important issues in patient care infrastructure include methods of data collection, whether monitoring is attended or unattended, who collects and analyzes the data, what is the patient care protocol, and what information becomes part of the medical record. More of these types of information was available on devices that transmit ECG data to attended monitoring centers (which includes all of the remote continuous attended monitoring devices). Attended monitoring centers are usually staffed by technicians (occasionally other health professionals) who analyze ECG data and report critical events to a patient's physician. Some centers send daily reports and/or a final summary report to the physician, and data are generally accessible to the physician at all times. The majority of patient- or event-activated intermittent recorders (looping or post-event) at least have the option of being attended by a fully-staffed monitoring center. Patient care protocols generally are not well described for most devices. However, stored ECG data are usually accessible by physicians during the monitoring period. The information that is incorporated into medical records was not clearly described in source documents for any of these devices, although we assume that, at a minimum, important events and diagnoses are entered into these records.

Overall Summary

This report is a systematic review focused on the downstream utility of a diagnostic technology. At a minimum, such a review needs to evaluate whether diagnosis actually leads to a change in clinical management, and ideally the review should evaluate whether the diagnosis ultimately leads to improved patient-oriented outcomes. Most of the studies in the field are focused on the question "does the technology lead to an

appropriate diagnosis,“ and any downstream outcomes are less likely to be reported. Some clinicians assume that a patient’s quality of life will improve simply from receiving a diagnosis, regardless of whether management is changed. However, this assumption remains an assumption in the absence of quality-of-life data obtained from validated instruments. While this report did find evidence that certain remote cardiac monitoring technologies lead to changes in patient management, the available evidence was insufficient to allow conclusions about the impact of remote cardiac monitoring technologies on any patient-oriented outcomes. Future studies that focus on downstream patient-oriented outcomes would be useful for determining the true benefit of these technologies.

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APPENDICES:

Supporting Documentation and Evidence Tables

Appendix A. Literature Searches

Electronic Database Searches

To obtain information for this report, we searched the following databases for relevant information:

Database	Date limits	Platform/provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1996 through November 7, 2007	OVID
The Cochrane Central Register of Controlled Trials (CENTRAL)	1996 through 2007, Issue 4	http://www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	1996 through 2007, Issue 4	http://www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	1996 through 2007, Issue 4	http://www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	1996 through 2007, Issue 4	http://www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1996 through November 7, 2007	OVID
Health Devices Alerts	1996 through February 8, 2007	ECRI
Health Technology Assessment Database (HTA)	1996 through 2007, Issue 4	http://www.thecochranelibrary.com
MEDLINE	1996 through November 7, 2007	OVID
metaRegister of Controlled Trials (mRCT)	Through November 29, 2007	http://www.controlled-trials.com/mrct/
PubMed (PreMEDLINE, Publisher)	Through November 7, 2007	http://pubmed.gov
U.K. National Health Service Economic Evaluation Database (NHS EED)	1996 through 2007, Issue 4	http://www.thecochranelibrary.com
U.S. Centers for Medicare & Medicaid (CMS) Web site	Through February 7, 2007	http://www.cms.gov Mediregs (www.coverageandpayment.com)
U.S. Food and Drug Administration (FDA) (adverse event reports)	1996 through November 29, 2007	http://www.fda.gov http://ecri.org
U.S. Food and Drug Administration (FDA) (product approval clearances)	1996 through November 29, 2007	http://www.fda.gov http://ecri.org
U.S. National Guideline Clearinghouse™ (NGC™)	Through February 9, 2007	http://www.ngc.gov

Hand Searches of Journal and Nonjournal Literature

Journals and supplements maintained in ECRI's collections were routinely reviewed. Nonjournal publications and conference proceedings from professional organizations, private agencies, and government agencies were also screened. Other mechanisms used to retrieve additional relevant information included review of bibliographies/ reference lists from peer-reviewed and gray literature. (Gray literature consists of reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in the peer-reviewed journal literature.)

- American College of Cardiology (ACC) Meeting Abstracts: 2004 - 2006
- American Heart Association (AHA) Meeting Abstracts: 2004
- Heart Rhythm Society (HRS) Meeting Abstracts: 2004 - 2006

Search Strategies

The search strategies employed combinations of freetext keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. The strategy below is presented in OVID syntax; the search was simultaneously conducted across EMBASE, MEDLINE, and PsycINFO. A parallel strategy was used to search the databases comprising the Cochrane Library.

Medical Subject Headings (MeSH), Emtree, PsycINFO and Keywords

Conventions:

OVID

$ = truncation character (wildcard)

exp = "explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)

.de. = limit controlled vocabulary heading

.fs. = floating subheading

.hw. = limit to heading word

.md. = type of methodology (PsycINFO)

.mp. = combined search fields (default if no fields are specified)

.pt. = publication Type

.ti. = limit to title

.tw. = limit to title and abstract fields

PubMed

[mh] = MeSH heading

[majr] = MeSH heading designated as major topic

[pt] = Publication Type

[sb] = Subset of PubMed database (PreMedline, Systematic, OldMedline)

[sh] = MeSH subheading (qualifiers used in conjunction with MeSH headings)

[tiab] = keyword in title or abstract

[tw] = Text word

CINAHL/EMBASE/MEDLINE
(English language, human)

Set Number	Concept	Search statement
1	Ambulatory ECG (controlled vocabulary)	Exp *electrocardiography, ambulatory/ or (Exp*electrocardiography monitoring/ and exp *ambulatory monitoring/)
2	ECG	Ecg.ti. or ekg.ti. or electrocardio$.ti. or exp *electrocardiography/ or *electrocardiogram/
3	Ambulatory	Ambulatory or home or remote or mobile cardiac outpatient telemetry or Exp telemetry/ or wireless or cellular phone.de. or mobile phone.de. or Bluetooth or zigbee or GSM or GPRS or telehealth$ or telemedicine or telecardiol$ or telemonit$ or Internet or web or computers, handheld.de. or computer communication networks.de. or ambient intelligence or pervasive computing or personal area network or continuous or real time or real-time or Event$.ti. or loop$ or insertable$ OR "pre-symptom" or "post-symptom" or ILR or memory or patient-activated
4	Specific names	CardioNet or HEARTlinkII or heart linkII or HEARTLink or Visicu or FlexNet or MCOT or eVital or EPI-MEDICS or HeartPOD or cardiophone$ or MobiHealth or TelePat or herz handy or vitaphone or "telemetry @ home" or CareLink or latitude or carenet or raytel cardiac services
5	Combine sets	1 or (2 and 3) or 4
6	Limit by publication type	5 not ((letter or editorial or news or comment or case reports or review or note or conference paper).de. or (letter or editorial or news or comment or case reports or review).pt.)
7	Clinical trials	6 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies or crossover procedure or double blind procedure or single blind procedure or placebo or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or random$.hw. or random$.ti. or placebo$.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (dummy or blind or sham)).mp. or latin square.mp. or ISRTCN.mp.)
8	Guidelines	6 and (st.fs. or guideline.pt. or consensus.pt. or practice parameter.mp. or position statement.mp. or position paper.mp. or policy statement.mp. or standard$.ti. or guideline$.ti. or white paper.mp. or clinical pathway.mp. or practice guidelines.de. or exp practice guideline/ or consensus development.de.)
9	Case reports	6 and (case reports.de. or case reports.pt. or case series.mp. or consequtive patient$.mp.)
10	Combine sets	or/7-9

PreMedline (PubMed)
(English language)

Set Number	Concept	Search statement
1	ECG	Ecg[ti] OR ekg[ti] OR electrocardio*[ti]
2	Ambulatory	Ambulatory OR home OR remote OR "mobile cardiac outpatient telemetry" OR telemetry OR wireless OR "cellular phone" OR "mobile phone" OR Bluetooth OR zigbee OR GSM OR GPRS OR telehealth* OR telemedicine OR telecardiol* OR telemonit* OR Internet OR web OR "ambient intelligence" OR "pervasive computing" OR "personal area network" OR continuous OR "real time" OR real-time OR Event*[ti] OR loop* OR insertable* OR "pre-symptom" OR "post-symptom" OR ILR OR memory OR patient-activated
3	Combine sets	#1 AND #2
4	Specific names	CardioNet OR HEARTlinkII OR heart linkII OR HEARTLink OR Visicu OR FlexNet OR MCOT OR eVital OR EPI-MEDICS OR HeartPOD OR cardiophone* OR MobiHealth OR TelePat OR "herz handy" OR vitaphone OR "telemetry @ home" OR CareLink OR latitude OR carenet OR "raytel cardiac services"
5	Combine sets	#3 OR #4
6	Limit to Premedline subfile	#5 AND (in process[sb] OR publisher[sb])

Appendix B. Quality of Literature and Evidence Strength Rating

Scales for Rating Individual Study Quality

For Key Question 3, all but three of the available studies that met the inclusion criteria of this report were uncontrolled before-after studies. Therefore, we used an 11-item scale specifically designed to evaluate the quality of before-after studies (see list of items below).

1. Was the study prospective?
2. Did the study enroll all patients or consecutive patients?
3. Were the criteria for including and excluding patients based on objective laboratory and/or clinical findings?
4. Were the patient inclusion/exclusion criteria established *a priori*?
5. Was the same initial treatment given to all patients enrolled?
6. Did all patients receive the same subsequent treatment(s)?
7. Was the outcome measure objective and was it objectively measured?
8. Did ≥85% of patients complete the study?
9. Were the characteristics of those who did and did not complete the study compared, and were these characteristics similar?
10. Was the funding for this study derived from a source that does not have a financial interest in its results?
11. Were the author's conclusions, as stated in the abstract or the article's discussion section supported by the data presented in the article's results section?

We used these items to compute a summary score, which ranges from 0 to 10, where 10 indicates an ideal study and 0 indicates a study of the poorest possible quality. To compute this summary score, we made the following calculations. We first converted

the individual item answers to numeric scores by counting 1 for each Yes answer, -1 for each No, and -0.5 for each NR. We then added the numeric scores for all 11 items, added 11 to the total, divided by 22, and multiplied by 10. These calculations yield the 0-10 summary scale described above. Studies that scored less than 5 were considered unacceptable quality, greater than or equal to 5 but less than 7.5 were considered low quality, and greater than or equal to 7.5 were considered moderate quality. Because we determined that control groups were necessary for accurate assessment of outcomes, uncontrolled before-after studies could not score above moderate quality.

Key Question 3 also included some controlled studies, and Key Question 4 required the use of controlled studies. The 25-item quality assessment instrument used to assess the quality of controlled studies that addressed these questions is presented below:

Comparability of Groups at Baseline

1. Were patients randomly assigned to the study's groups?
2. Did the study employ stochastic randomization?
3. Were any methods other than randomization used to make the patients in the study's groups comparable?
4. Were patients assigned to groups based on factors other than patient or physician preference?
5. Were the characteristics of patients in the different study groups comparable at the time they were assigned to groups?
6. Did patients in the different study groups have similar levels of performance on all of the outcome variables at the time they were assigned to groups?
7. Was the comparison of interest prospectively planned?
8. Did ≥85% of the patients complete the study?
9. Was there a ≤15% difference in completion rates in the study's groups?
10. Were all of the study's groups concurrently treated?
11. Was compliance with treatment ≥85% in both of the study's groups?
12. Was there concealment of allocation?

Blinding

13. Were subjects blinded to the treatment they received?
14. Did the authors perform any tests after completing the study to ensure that the integrity of the blinding of patients was maintained throughout the study?
15. Was the treating physician blinded to the groups to which the patients were assigned?
16. Were those who assessed the patient's outcomes blinded to the group to which the patients were assigned?

Measurement/Instrument

17. Was the outcome measure of interest objective and was it objectively measured?
18. Were the same laboratory tests, clinical findings, psychological instruments, etc., used to measure the outcomes in all of the study's groups?
19. Was the instrument used to measure the outcome standard?
20. Were the follow-up times in all of the study's relevant groups approximately equal?

Treatment

21. Was the same treatment given to all patients enrolled in the experimental group?
22. Was the same treatment given to all patients enrolled in the control group?
23. Were all of the study's groups treated at the same center?

Investigator Bias

24. Was the funding for this study derived from a source that does not have a financial interest in its results?
25. Were the author's conclusions, as stated in the abstract or the article's discussion section, supported by the data presented in the article's results section?

We used these items to compute a summary score, which ranges from 0 to 10, where 10 indicates an ideal study and 0 indicates a study of the poorest possible quality.

To compute this summary score, we made the following calculations. We first converted the individual item answers to numeric scores by counting 1 for each Yes answer, -1 for each No, and -0.5 for each NR. We then added the numeric scores for all 25 items, added 25 to the total, divided by 50, and multiplied by 10. These calculations yield the 0-10 summary scale described above. Studies that scored less than 5 were considered unacceptable quality, greater than or equal to 5 but less than or equal to 6.7 were considered low quality, greater than 6.7 but less than or equal to 8.4 were considered moderate quality, and 8.5 or greater were considered high quality.

Strength of Evidence System

After grading the body of evidence for a particular question on each of several decision points (listed in the next sections), we apply the grades to a system that divides the strength of the evidence supporting each conclusion into one of four categories: strong, moderate, weak, or inconclusive. Table B-1 illustrates how these categories relate to qualitative and quantitative conclusions.

Table B-1. Interpretation of Different Categories of Strength of Evidence Supporting Conclusion

Strength of Evidence	Interpretation of Qualitative Conclusion
Strong	Evidence supporting the qualitative conclusion is convincing. It is highly unlikely that new evidence will lead to a change in this conclusion.
Moderate	Evidence supporting the qualitative conclusion is somewhat convincing. There is a small chance that new evidence will overturn or strengthen our conclusion. ECRI recommends regular monitoring of the relevant literature at this time.
Weak	Although some evidence exists to support the qualitative conclusion, this evidence is tentative and perishable. There is a reasonable chance that new evidence will overturn or strengthen our conclusions. ECRI recommends frequent monitoring of the relevant literature at this time.
Inconclusive	Although some evidence exists, this evidence is not of sufficient strength to warrant drawing an evidence-based conclusion from it. ECRI recommends frequent monitoring of the relevant literature at this time.
Stability of Evidence	Interpretation of Quantitative Conclusion
High	The estimate of treatment effect included in the conclusion is stable. It is highly unlikely that the magnitude of this estimate will change substantially as a result of the publication of new evidence.
Moderate	The estimate of treatment effect included in the conclusion is somewhat stable. There is a small chance that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI recommends regular monitoring of the relevant literature at this time.
Low	The estimate of treatment effect included in the conclusion is likely to be unstable. There is a reasonable chance that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI recommends frequent monitoring of the relevant literature at this time.
Unstable	Estimates of the treatment effect are too unstable to allow a quantitative conclusion to be drawn at this time. ECRI recommends frequent monitoring of the relevant literature.

To arrive at these strength-of-evidence categories, we applied the ECRI Strength of Evidence System. Additional information on this system appears in a recent publication.(69) This system, which appears in Figure 3 through Figure 6 below, involves 10 decision points. The methods we used to resolve these 10 decision points appear below. In this report, decision points 1, 2, 3, and 8 were the only decisions that were necessary given the available evidence bases.

Decision Point #1: Acceptable Quality

The above section entitled Study Quality Scale describes our approach to determining whether each study was of acceptable quality.

Decision Point #2: Overall Quality

After assigning quality scores to each individual study, we then classified the overall quality of the evidence base by taking the median of the Overall quality scores. Quality scores were converted to categories as defined in Table B-2. For example, if the evidence base consists of four studies with overall scores of 6.5, 7, 7.9, and 9, then the median is 7.6 and the overall evidence base is considered moderate quality. The definitions for what constitutes low, moderate, or high quality evidence were determined *a priori* by a committee of three methodologists. If the median quality was on the border between categories, we took the lower quality category as the overall quality. Because we determined that control groups were necessary for accurate assessment of outcomes, uncontrolled case series could not score above moderate quality.

Table B-2. Categorization of Quality

Study design	High quality	Moderate quality	Low quality
Controlled trials	≥8.5	≥6.8 but <8.5	≥5 but <6.8
Before-after studies (case series)	Not applicable	≥7.5	≥5 but <7.5

Decision Point #3: Does Reporting Allow Quantitative Conclusions to be Reached?

The answer to Decision Point 3 depends upon the adequacy of reporting in available studies as well as the number of available studies. In order to conduct a quantitative analysis of a given outcome, the data for that outcome must be reported in at least three studies in a manner that allows the data to be pooled in a meta-analysis. If less than three studies are available, no quantitative conclusion is reached regardless of reporting. Another situation that does not allow a quantitative conclusion is when three or more studies are available, but fewer than 80% of them permit determination of the effect size and its dispersion, either by direct reporting from the trial or calculations based on reported information. If no quantitative conclusion is possible, then one moves directly to Decision Point 8 to begin a qualitative analysis.

Decision Point #4: Are Data Quantitatively Consistent (Homogeneous)?

This decision point is used only if the answer to Decision Point 3 was Yes. Consistency refers to the extent to which the results of studies in an evidence base agree with each other.(70) The more consistent the evidence, the more precise a summary estimate of treatment effect derived from the evidence base. Quantitative consistency refers to consistency tested in a meta-analysis using the Q statistic and Higgins and Thompson's I^2 statistic.(26) We consider the evidence base to be quantitatively consistent when I^2 <50%.

If the studies are homogeneous, we combine the results in a random-effects meta-analysis (REMA). We then determine whether the summary effect size is informative or non-informative. The summary effect is considered informative if it meets any one of the following three criteria:

1) The summary effect is statistically significant.
2) If the minimum boundary of clinical significance is greater than 0, the 95% confidence intervals of the summary effect must exclude the possibility of a clinically significant effect.

3) If the boundary of clinical significance equals 0 (clinical significance = statistical significance), the 95% confidence intervals of the summary effect must not overlap with -0.2 or +0.2 (this assumes one is using Hedges' g or Cohen's h as the meta-analytic summary statistic).

Criteria 2) and 3) require definitions of the minimum difference between treatments (or between baseline and post-treatment measurements) that is considered clinically significant. The definitions that we used appear in Table B-3.

Table B-3. Definitions of Clinical Significance

Outcome	Minimum effect considered to be clinically significant
Key Questions 3, 4, 5	
Palpitations, syncopal episodes, TIAs and non-fatal stroke, dizziness, dyspnea or heart failure, angina or MI, mortality	Any statistically significant difference
Quality of life	A difference of 0.2 using Hedges' g

If the summary effect is informative, we then test the stability of the findings in Decision Point 5.

Decision Point #5: Are Findings Stable (Quantitatively Robust)?

Stability of findings refers to the likelihood that a summary effect estimate will be substantially altered by changing the conditions of the analysis. If a quantitative analysis was possible, stability would be tested by several methods of sensitivity analysis, including removal of each individual study separately, changing the effect size measure (e.g., from odds ratio to Cohen's h), and cumulative meta-analysis by publication date (described in more detail below). If one of these analyses overturns the findings of the primary meta-analysis, the findings are not robust.

Decision Point #6: Meta-regression Explains Heterogeneity?

Meta-analyses with heterogeneity are further evaluated with meta-regression. Meta-regression is not performed on a low quality evidence base. Heterogeneity is assessed by meta-regression using the permutation test method of Higgins and Thompson (2004)(71) and the meta-regression module in the Stata software

package.(72) Meta-regression was only performed if there were 10 or more studies in an evidence base with an average quality that was moderate or high,(73) and a precise effect size could be calculated from at least 75% of the studies.

Decision Point #7: Meta-regression Model Robust?

If heterogeneity can be explained with meta-regression does the model hold through sensitivity testing? Testing would involve removal of each individual study from the meta-regression to determine whether removal of any single study changes the results of the meta-regression.

Decision Point #8: Qualitatively Robust?

If the evidence base for an outcome had three or more studies, we performed a random-effects meta-analysis (REMA) and determined whether the qualitative findings could be overturned by removal of any single study, cumulative meta-analysis by publication date, or by changing the assumed success rate in the control groups (this imputation is described in more detail in the text under Key Question 3). We considered findings to be overturned only when a sensitivity analysis altered the conclusion (i.e., a statistically significant finding becomes non-significant as studies are added to the evidence base).

Decision Point #9: Qualitatively Consistent?

This Decision Point is used only when the evidence base for an outcome consists of two studies. For a given outcome, studies were considered qualitatively consistent if both studies had a statistically significant effect in the same direction, or if both studies did not have a statistically significant effect.

Decision Point #10: Magnitude of Effect Extremely Large?

When considering the strength of evidence supporting a qualitative conclusion based on only one or two studies, magnitude of effect becomes very important. If a single study finds a large effect with a narrow confidence interval, then new evidence is unlikely to overturn the qualitative conclusion. To resolve this decision point, we consulted the

effect size and the 95% confidence interval around the effect size for the study (with two studies, we consulted the interval around the random effects summary statistic). If this interval was an odds ratio fully above +2.5 (or if it was fully below -2.5) and the effect size was ≥4.5 (or ≤-4.5), we considered the effect to be large. Otherwise, we considered it to be not large. For example, an interval from +3 to +11 would be considered a large effect, whereas an interval from +2 to +13 would not be considered a large effect. Another effect that would be considered large is an interval from -3 to -11 (large in the negative direction). If one is using the standardized mean difference (Hedges' g) as the measure of effect, the values for a moderate and large effect are 0.5 and 0.8, respectively. The choice of 0.5 and 0.8 is based on Cohen,(74) who stated that an effect size of 0.5 was "moderate" and 0.8 was "large"; thus the decision rule required that the effect be statistically significantly larger than "moderate".

Figure 3. General Section of Strength-of-Evidence System

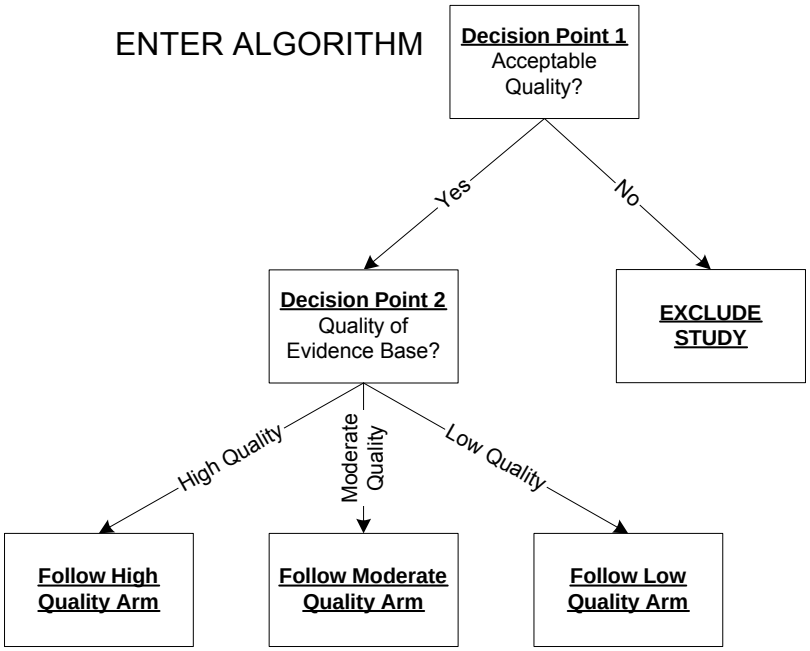


Figure 4. High Quality Arm of Strength-of-Evidence System

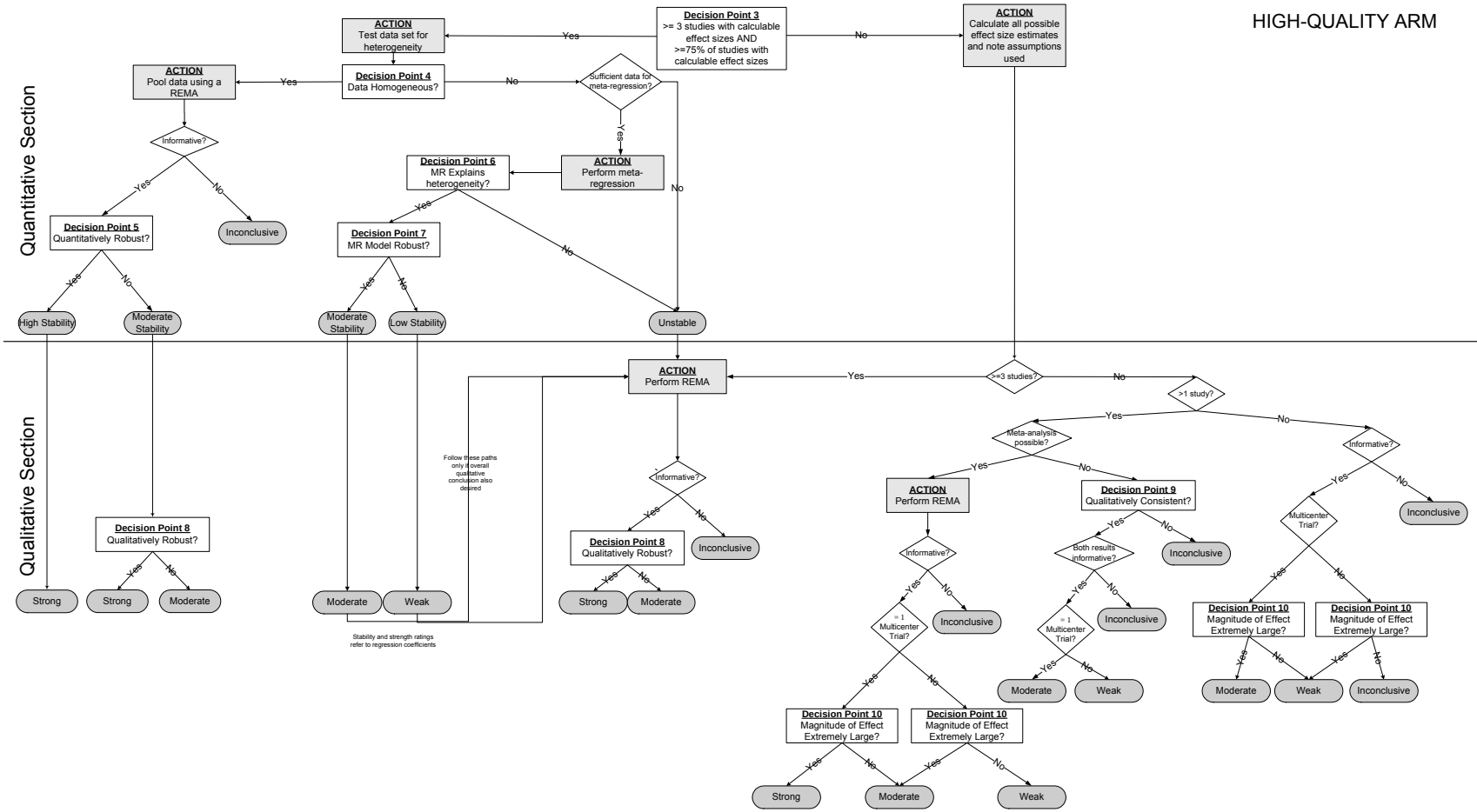


Figure 5. Moderate Quality Arm of Strength-of-Evidence System

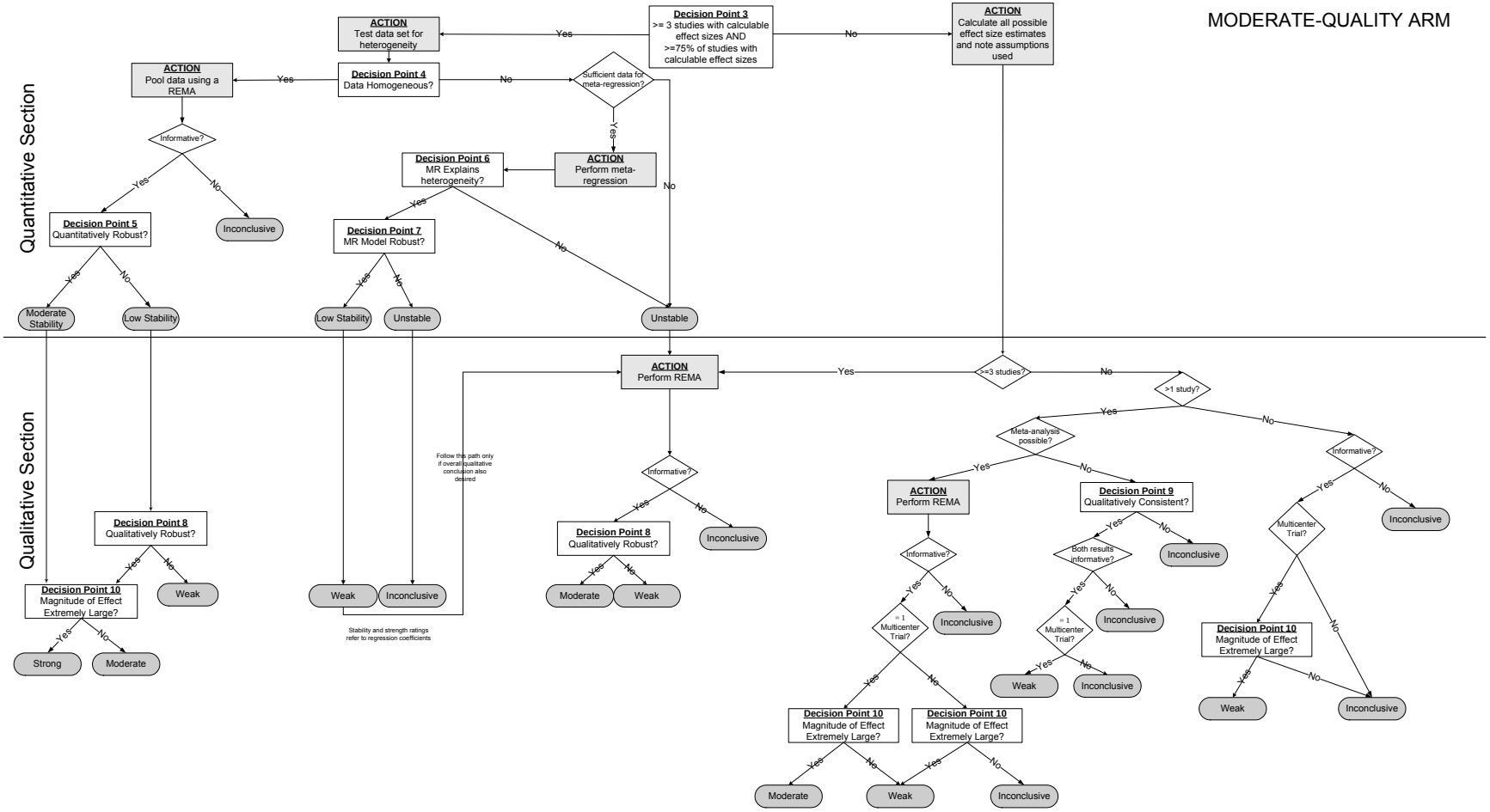
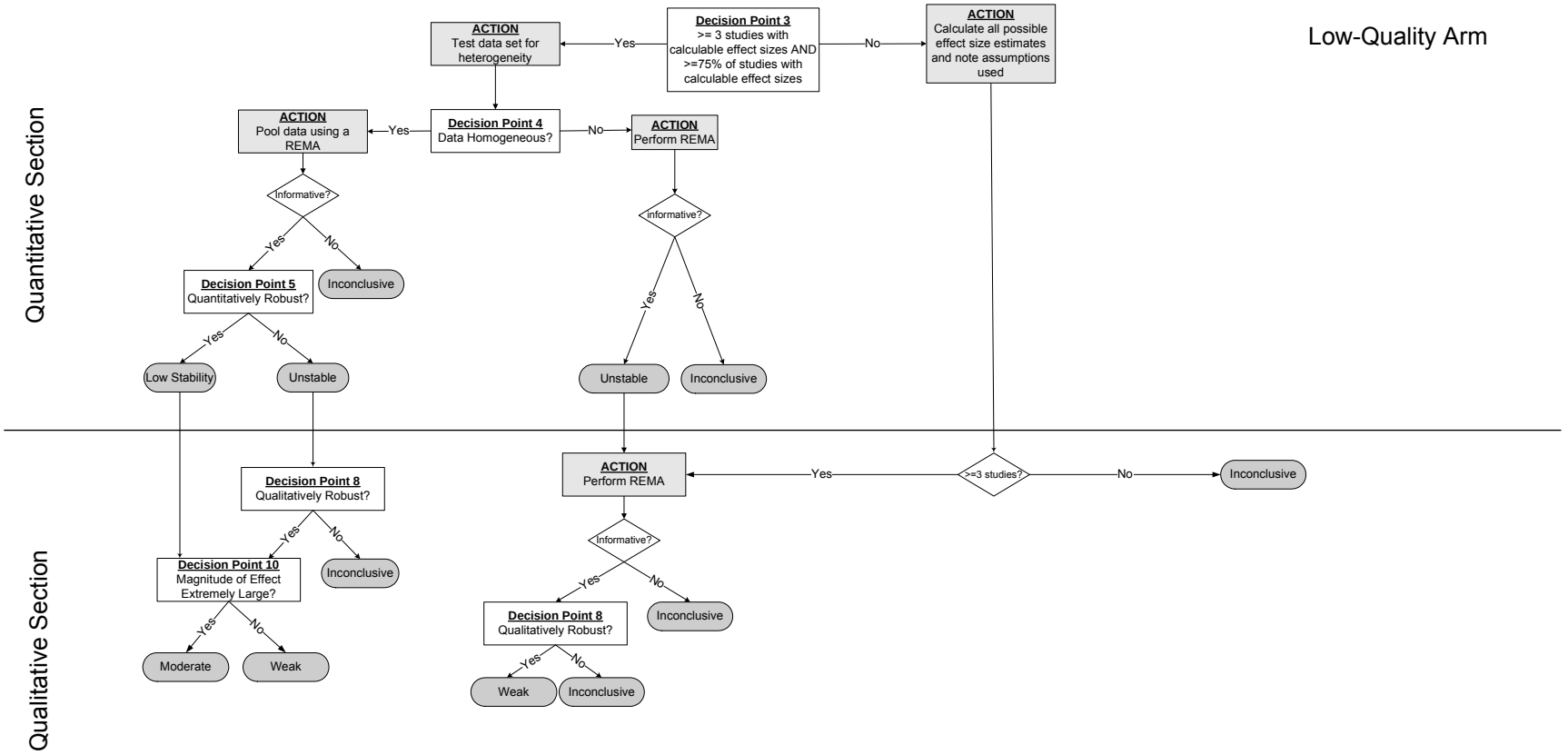


Figure 6. Low Quality Arm of Strength-of-Evidence System



Appendix C. Characteristics of Remote Cardiac Monitoring Devices

Table C-1. Characteristics of Remote Cardiac Monitoring Devices

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
Patient or event-activated external loop recorders (ELR)						
ER900 Series Cardiac Event Monitors(75,76)	Advanced Biosensor (Columbia, SC, USA) www.advancedbiosensor.com Braemar Inc. (Eagan, MN, USA) www.braemarinc.com	2	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: 30 minutes (records up to 30 events) Battery life: 1 month	Transtelephonic or direct-to-PC	
ER900L Cardiac Event Monitor(77)	Braemar Inc. (Eagan, MN, USA) www.braemarinc.com	1	Patient-activated (for symptomatic events)	Memory: 512 seconds Battery life: 1 month plus	Transtelephonic or direct-to-PC	
Heart 2005A™ Transtelephonic ECG Loop Event Recorder(78)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com Cardiac Telecom (Greensburg, PA, USA) www.cardiactelecom.com	1	Patient-activated (for symptomatic events)	Memory: 240 seconds Battery life: 1 month	Transtelephonic transmission of ECG data to central monitoring lab.	
Heart 2006™ Dual-Lead Transtelephonic ECG Loop Event Recorder(79)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com	2	Patient-activated (for symptomatic events)	Memory: 480 seconds (records up to 8 events) Battery life: 1 month	Transtelephonic transmission of ECG data to central monitoring lab.	

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
HeartView™ 12-Lead ECG Recorder/ Transmitter(80)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com	12	Patient-activated (for symptomatic events)	Memory: records a 12-lead ECG simultaneously (2.5 seconds/lead and 10 seconds of rhythm lead) Battery life: 1 month	Transtelephonic or digital transmission of ECG data to central monitoring lab.	
HeartView P12/8 PlusTM 12/8 ECG Personal Recorder/ Transmitter(81)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com	8 or 12	Patient-activated (for symptomatic events)	Memory: records a 12-lead ECG simultaneously (2.5 seconds/lead (4 seconds optional) and 10 seconds of rhythm lead) Battery life: 1 month	Transtelephonic or digital transmission of ECG data to central monitoring lab.	
CG-6106 Personal 1-Lead ECG Monitor(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	1	Patient-activated (for symptomatic events)	Memory: 522 seconds Battery life: 1,500 hours	Transtelephonic transmission of ECG data.	
Genesis™(83)	Cardiac Evaluation Center (Milwaukee, WI) www.cec.net Lechnologies Research (Sussex, WI) www.lechnologies.com	1 or 2	Patient-activated (for symptomatic events)	Memory: 8 minutes (records up to 8 events) Battery life: >30 days	Transtelephonic transmission of ECG data.	Attended
Cardiophonics 1000 Memory Monitor(78,84)	Cardiophonics (Timonium, MD) www.cardiophonics.com	2	Patient-activated (for symptomatic events)	Memory: NR Battery life: at least 30 days	Transtelephonic transmission of ECG data. To an attended monitoring station (24/7).	Attended (technicians)
E-Tac EX-1000 ECG Event Recorder(85)	Datrix (Escondido, CA) (no web address identified)	1	Patient-activated (for symptomatic events)	Memory: 360 seconds Battery life: up to 30 days (2 AAA batteries)	Transtelephonic transmission of stored ECG data	

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
TTM5000 Telephonic EKG Monitor(86)	HDS Medical (Laguna Niguel, CA) (Web site being remodeled)	NR	Patient-activated (for symptomatic events)	Memory: NR Battery life: NR	Transtelephonic transmission of ECG data	
King of Hearts Express® Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	1	Patient-activated (for symptomatic events)	Memory: 300 seconds (records up to 60 events) Battery life: 7 days (continuous use)	Transtelephonic transmission of ECG data	Intended for diagnosis of transient symptoms (dizziness, palpitations, chest pain).
King of Hearts Express®+ Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	1	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: 600 seconds Battery life: 7 days (with continuous use)	Transtelephonic transmission of ECG data	Detects bradycardia and tachycardia
King of Hearts Express® AF Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	1	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: 600 seconds (records up to 60 events) Battery life: 7 days (with continuous use)	Transtelephonic or wireless (cell phone) transmission of ECG data.	Detects AF, bradycardia, and tachycardia
MicroLR® Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	1	Patient-activated (for symptomatic events)	Memory: 524 seconds (records up to 6 events) Battery life: 1,000 hours (in loop mode)	Transtelephonic transmission of ECG data.	
LifeStar AF Express(88,89)	Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	1	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: 10 minutes Battery life: at least 30 days	Transtelephonic transmission of ECG data.	Detects AF, tachycardia, and bradycardia Attended (cardiac technicians)

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
LifeStar AF Express(88,89)	Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	1 or 3	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: 18 minutes Battery life: at least 30 days	Transtelephonic transmission of ECG data	Detects AF, tachycardia, bradycardia, and cardiac pause Attended (cardiac technicians)
LifeWatch Explorer(88,89)	Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	1	Patient-activated (for symptomatic events)	Memory: 524 seconds Battery life: at least 30 days	Transtelephonic transmission of ECG data	Attended (cardiac technicians)
PER (Personal ECG Recorder)(90,91)	Medical Monitors Ltd. (Eastgardens, Australia) www.medmon.com.au	1	Patient-activated (for symptomatic events)	Memory: 160 seconds (records up to 2 events before transmission required) Battery life: >1,400 hours (continuous monitoring)	Transtelephonic transmission of ECG data to a central monitoring station (Cardiocom).	
CardioPAL SAVI™ Event Monitor(92)	Medicomp (Melbourne, FL, USA) www.medicompinc.com	1 or 2	Automatic activation by asymptomatic and symptomatic arrhythmias	Memory: 20 minutes Battery life: NR, but FDA document states device can be worn for weeks.	Transtelephonic transmission of ECG data to a cardiac monitoring center.	Captures rate, rhythm, morphology, and p-wave analysis to identify meaningful events. P-wave analysis provides the ability to auto-capture atrial arrhythmias. Attended
CardioPAL AI™ Event Monitor(92,93)	Medicomp (Melbourne, FL, USA) www.medicompinc.com	1 or 2	Automatic activation by asymptomatic and symptomatic arrhythmias	Memory: 20 minutes Battery life: NR, but FDA document states device can be worn for weeks.	Transtelephonic transmission of ECG data to a cardiac monitoring center.	Diogenes Holter system uses R^2M technology to compare rate, rhythm and morphology to identify meaningful events. Attended

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
CardioPAL™ Event Monitor(92)	Medicomp (Melbourne, FL, USA) www.medicompinc.com	1	Automatic activation by asymptomatic and symptomatic arrhythmias	Memory: 20 minutes Battery life: NR	Transtelephonic transmission of ECG data to a cardiac monitoring center.	Patients can record through leads attached to fingertips if chest electrodes become uncomfortable. ECG strips can be processed through Diogenes Holter system; R^2M technology compares rate, rhythm and morphology to identify meaningful events. Attended
DR200E "Tel-a-heart"™ Event Recorder(94,95)	Northeast Monitoring (Maynard, MA) www.nemon.com	1 or 2	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: 90 minutes Battery life: 30 days	Transtelephonic or digital transmission of ECG data	
R. Test Evolution 3 Event Monitor(96,97)	Novacor (Cedex, France) www.novacor.com	1	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: 20 minutes Battery life: up to 8 days	Transtelephonic transmission of ECG data. Software option allows transmission via modem or e-mail.	
River-1 Electrocardiograph (ECG) Recorder and Transmitter(98)	SHL Telemedicine (Tel Aviv, Israel) www.shl-telemedicine.com	1, 2, or 3	Patient-activated (for symptomatic events)	Memory: NR Battery life: NR	Transtelephonic or digital transmission of ECG data	
Heart Aide EZd(99,100)	TZ Medical (Portland, OR) www.tzmedical.com	1 or 2	Patient-activated (for symptomatic events)	Memory: NR Battery life: up to 28 days	Transtelephonic transmission of ECG data	
Hearttrak Smart AT and Hearttrak Smart²(101)	Universal Medical (Ewing, NJ) (no web address identified)	NR	Patient-activated (for symptomatic events)	Memory: NR Battery life: NR	Transtelephonic transmission of ECG data	

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
Vitaphone 3100 BT 1-Channel ECG Loop Recorder(102)	Vitasystems GmbH (Chemnitz, Germany) www.telemedsys.de/en	1	Automatic activation by asymptomatic and symptomatic arrhythmias	Memory: 42 minutes Battery life: NR	Wireless transmission of ECG data via Bluetooth™ technology.	Automatic detection of bradycardia, tachycardia, AF, and cardiac pause.
Vitaphone 3300 BT 3-Channel ECG Loop Recorder(103)	Vitasystems GmbH (Chemnitz, Germany) www.telemedsys.de/en	3	Automatic activation by asymptomatic and symptomatic arrhythmias	Memory: 20 minutes Battery life: NR	Wireless transmission of ECG data via Bluetooth™ technology.	Automatic detection of bradycardia, tachycardia, AF, and cardiac pause.
Cardiocall 20 and VS20 event recorders (can be used as loop recorder or post-event recorder)(104,105)	Delmar Reynolds Medical (Irvine, CA) www.delmarreynoldscom	1 or 2	Patient-activated (for symptomatic events)	Memory: 20 minutes (records up to 10 events in looping mode) Battery life: NR	Transtelephonic transmission or download of ECG data into a PC.	
eTrigger™ AF 920 (available in both looping and non-looping models)(106)	eCardio (Woodlands, TX) www.ecardio.com	NR	Automatic activation by asymptomatic AF	Memory: 30 minutes (looping mode) Battery life: 30 days	Transtelephonic transmission of ECG data.	Attended (certified technicians)
Patient or event-activated insertable loop recorders (ILR)						
REVEAL® PLUS Insertable Loop Recorder(32)	Medtronic (Minneapolis, MN, USA) www.medtronic.com	NR	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: 42 minutes Battery life: at least 14 months	None. Office visit required for analysis of ECG data. (retrieval and analysis by Medtronic Programmer system)	Detects asystolic pauses, bradycardia, and tachycardia. Not attended
SLEUTH™ Implantable ECG Monitoring System(33)	Transoma Medical (Arden Hills, MN) www.transomamedical.com	NR	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: NR Battery life: at least 14 months	Wireless transmission of ECG data.	Attended

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
Post-event recorders						
PER900 Post Event Recorder(107,108)	Advanced Biosensor (Columbia, SC, USA) www.advancedbiosensor.com Braemar Inc. (Eagan, MN, USA) www.braemarinc.com	1	Patient-activated (for symptomatic events)	Memory: 30 minutes Battery life: 1 month	Transtelephonic transmission of ECG data	
HeartOne™(109)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com	1	Patient-activated (for symptomatic events)	Memory: 120 seconds (stores up to 4 events) Battery life: NR	Transtelephonic transmission of ECG data to a central receiving station	
CG-2206 Personal 1-Lead ECG Monitor(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	NR	Patient-activated (for symptomatic events)	Memory: Records and stores up to 6 events Battery life: NR	Transtelephonic transmission of ECG data	
CG-5000 Minimonitor Transmitter(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	NR	Patient-activated (for symptomatic events)	Memory: stores up to 6 events Battery life: NR	Transtelephonic transmission of ECG data	
PMP^4 SelfCheck™ ECG(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	1 or 12	Patient-activated (for symptomatic events)	Memory: records 1 channel in 32 seconds, 12 channel in 5 seconds, total memory not reported Battery life: 970 transmissions	During self-monitoring, the results are continuously transmitted to a PDA or cell phone during test performance via wireless Bluetooth technology. The data can then be transmitted wirelessly to the PMP Web Center and stored for review by physician or patient	Patient self-monitoring of symptoms such as skipped beats, palpitations, racing heart, irregular pulse, faintness. The patient holds the device to their chest for 30 seconds and records the ECG. Wireless transmission sets this apart from other post-event monitors.

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
CG-7100 Personal 12-Lead ECG Recorder(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	8 or 12	Patient-activated (for symptomatic events)	Memory: records 8 channel in 20 seconds, 12-channel in 41 seconds Battery life: >600 sessions	Transtelephonic transmission of ECG data to a receiving station.	Includes pacemaker pulse marker. Intended to monitor gross cardiac morphology changes.
ecg@home(110)	H & C Medical Devices (Milan, Italy) (no web address identified)	1	Patient-activated (for symptomatic events)	Memory: 200 seconds Battery life: 2,400 recordings	Transtelephonic transmission or download of ECG data to PC	
MEMORYTRACE™ Model 4224 Ambulatory ECG(111)	Hi-tronics Designs (Budd Lake, NJ) www.hitronics.com	NR	Patient-activated (for symptomatic events)	Memory: NR Battery life: NR	Transtelephonic transmission of ECG data	
MicroER® Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	1	Patient-activated (for symptomatic events)	Memory: 192 seconds (stores up to 6 events) Battery life: 2,000 sessions	Transtelephonic transmission of ECG data	
LifeWatch ER(88,89)	Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	1	Patient-activated (for symptomatic events)	Memory: 186 seconds Battery life: at least 30 days	Transtelephonic transmission of ECG data	Attended (cardiac technicians)
Micro™ ECG Recorder(112)	Medical Monitors Ltd. (Eastgardens, Australia) www.medmon.com.au	1	Patient-activated (for symptomatic events)	Memory: 80 seconds (records up to 2 events before transmission required) Battery life: 2,500 transmissions	Transtelephonic transmission of ECG data to a central monitoring station (Cardiocom)	
Cardiobeeper CB - 12/12(113,114)	SHL Telemedicine (Tel Aviv, Israel) www.shl-telemedicine.com	3 (with 12-lead ECG)	Patient-activated (for symptomatic events)	Memory: NR Battery life: NR	Transtelephonic transmission of ECG data	Attended

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
Cardiobeeper CB - 12L(115,116)	SHL Telemedicine (Tel Aviv, Israel) www.shl-telemedicine.com	NR, but 12-lead ECG	Patient-activated (for symptomatic events)	Memory: NR Battery life: NR	Transtelephonic transmission of ECG data	Attended
Heart Aide(99,100)	TZ Medical (Portland, OR) www.tzmedical.com	1	Patient-activated (for symptomatic events)	Memory: 270 seconds Battery life: up to 1 year	Transtelephonic transmission of ECG data	
Vitaphone 100 IR ECG Post-Event Recorder(117)	Vitasystems GmbH (Chemnitz, Germany) www.telemedsys.de/en	1	Patient-activated (for symptomatic events)	Memory: 90 seconds (records up to 3 events) Battery life: reported to last for 5 years, but not clear if this reflects constant usage.	Digital transmission of ECG data via infrared wireless link. Not attended.	
eTrigger™ AF 920 (available in both looping and non-looping models)(106)	eCardio (Woodlands, TX) www.ecardio.com	NR	Automatic activation by asymptomatic AF	Memory: NR Battery life: 30 days	Transtelephonic transmission of ECG data	Attended (certified technicians)
Cardiocall event recorder (can be used as loop recorder or post-event recorder)(104,105)	Delmar Reynolds Medical (Irvine, CA) www.delmarreynoldscom	NR	Patient-activated (for symptomatic events)	Memory: NR Battery life: NR	Transtelephonic transmission or download of ECG data into a PC	

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
Real-time continuous attended cardiac monitors						
CardioNet Mobile Cardiac Outpatient Telemetry (MCOT) System(18)	CardioNet, Inc. (San Diego, CA, USA) www.cardionet.com	3	Automatic arrhythmia activation, can be programmed to perform as a Holter monitor or as a looping event recorder. Also can be patient-activated (for symptomatic events)	Memory: 24 hours (continuous) Battery life: up to 21 days	Transtelephonic or cellular (wireless) transmission of ECG data to central monitoring station.	Transmits data automatically when ECG threshold exceeded, hence "real-time". Attended (certified technicians)
HEARTLink II arrhythmia detector and alarm system(1,118)	Cardiac Telecom (Greensburg, PA, USA) www.cardiactelecom.com	1	Automatic activation and patient-activated (for symptomatic events)	Memory: 30 minutes Battery life: NR	Processes radiofrequency-encoded transmitted ECG signals on the Tele-Link monitoring unit, which transmits them via telephone to a central monitoring lab.	Device has 4 operational modes: real-time automatic event mode, real-time display mode, patient-activated mode for symptomatic events and a help request. The system also has pacemaker pulse detection and reporting. Transmits data automatically when arrhythmia detected, hence "real-time". Attended (certified technicians)
VST™ (Vital Signs Transmitter)(2,19)	Biowatch Medical (Grand Rapids, MI) www.biowatchmed.com	NR	Automatic arrhythmia activation	Memory: 32 hours Battery life: NR	Transmission by cellular modem to central monitoring station	Critical events automatically transmitted to Biowatch central monitoring center, hence "real-time". Attended (nurses or critical care specialists)

Device name	Manufacturer	Number of channels	Activation (automatic, patient-activated, or both)	Memory (ECG storage capacity) and battery life	Type of ECG transmission	Other comments
CG-6108 ACT (Ambulatory Cardiac Telemetry)(82) Also known as: LifeStar ACT™(119)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com Also marketed by: Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	NR	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: NR Battery life: at least 21 days	Transtelephonic or wireless (cell phone) transmission of ECG data. Automatically transmits to Life Watch monitroring center when an arrhythmia is detected.	Automatically detects AF, bradyarrhythmia, tachyarrhythmia, and cardiac pause. Attended (cardiac technicians)
Other devices – monitors with event-recording and Holter monitoring characteristics						
C.Net 2100 Monitor(120)	Cardionetics (Hampshire, UK) www.cardionetics.com	NR	Patient-activated (for symptomatic events) Also can record continuously for 24 h similar to Holter monitor.	Memory: Records up to 10 events per 24 hr period Battery life: NR	No transmission during monitoring period. ECG data downloaded to printer in physician's office at end of monitoring period.	Not attended
DR200/HE Holter and Event Recorder(95,121)	Northeast Monitoring (Maynard, MA) www.nemon.com	NR	Automatic arrhythmia activation and patient-activated (for symptomatic events)	Memory: NR Battery life: NR, but can record continuously in Holter mode for 14 days	Transtelephonic or digital transmission of ECG data	
Pelex-04 Wireless ECG(122,123)	Pinmed (Pittsburgh, PA) www.pinmed.net	12	Patient-activated (for symptomatic events or periodic monitoring during activities). Also can record continuously similar to Holter monitor.	Memory:Varies depending upon configuration. Maximum 72 hours. Battery life: up to several weeks	Transtelephonic, wireless, Wi-Fi, or Internet transmission of ECG data	Patient self-monitoring during various activities (e.g., exercise, daily activities)

NA – Not applicable.
NR – Not reported.

Appendix D. Summary Evidence Tables

Table D-1. Excluded Studies

Reference	Year	Reason for exclusion
Key Question 3		
Hoefman et al.(124)	2007	No relevant outcomes reported
Olson et al.(125)	2007	No relevant outcomes reported
Hoch et al.(126)	2006	No relevant outcomes reported
Alte et al.(127)	2005	No relevant outcomes reported
Hoefman et al.(128)	2005	No relevant outcomes reported
Reiffel et al.(129)	2005	No relevant outcomes reported
Rockx et al.(130)	2005	No relevant outcomes reported
Scalvini et al.(131)	2005	No relevant outcomes reported
Senatore et al.(132)	2005	No relevant outcomes reported
Farwell et al.(34)	2004	Patient overlap with an included study(10)
Gula et al.(35)	2004	No relevant outcomes reported
Israel et al.(133)	2004	No relevant outcomes reported
Rugg-Gunn et al.(134)	2004	Patients had confirmed epilepsy, a condition beyond the scope of the report
Saarel et al.(135)	2004	Different classes of recorders analyzed together
Solano et al.(136)	2004	Patient overlap with an included study(56)
Assar et al.(137)	2003	No relevant outcomes reported
Barthelemy et al.(138)	2003	No relevant outcomes reported

Reference	Year	Reason for exclusion
Huikuri et al.(37)	2003	Cannot tell when certain events occurred, which events would not have been detected by Holter or ILR
Schuchert et al.(139)	2003	No relevant outcomes reported
Sivakumaran et al.(36)	2003	No relevant outcomes reported
Wu et al.(140)	2003	No relevant outcomes reported
Krahn et al.(141)	2002	Patient overlap with an included study
Brignole et al.(142)	2001	Patient overlap with an included study
Makowska et al.(143)	2000	No relevant outcomes reported
Swerdlow et al.(144)	2000	No relevant outcomes reported
Zaidi et al.(145)	2000	Only a small fraction of patients received a remote monitoring device, outcomes not adequately separated from outcomes of patients who received other tests.
Krahn et al.(146)	1999	Patient overlap with an included study(62)
Keller(147)	1998	No relevant outcomes reported
Krahn et al.(148)	1998	Patient overlap with an included study(64)
Zimetbaum et al.(149)	1998	No relevant outcomes reported
Fogel et al.(150)	1997	No relevant outcomes reported
Krahn et al.(151)	1997	No relevant outcomes reported
Roche et al.(152)	1997	Does not report how many patients diagnosed in first 24 hours
Zimetbaum et al.(153)	1997	No relevant outcomes reported
Key Question 4		
Krahn et al.(154)	2003	Incomplete reporting of results and patient overlap with an included study(61)

Table D-2. Summary of Included Studies (Key Question 3)

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Studies of insertable loop recorders (ILR)				
Farwell et al. 2006(10)	Design: Randomized controlled trial Purpose: To determine the clinical and cost-effectiveness of an ILR in the management of recurrent syncope in an unselected patient population with recurrent syncope ECRI Quality Score (Rating): 8.1 (Moderate)	Monitor: Reveal Plus ILR Control: Conventional assessment (not described in study)	Total Enrolled: 201 Age mean (range) Median 74 (59.1 to 80.7) % female: 54 Inclusion Criteria: Consectutive patients of age ≥16 years, acute syncope presentation, ≥2 unexplained syncopes in the past 12 months, no pacing indication following basic clinical workup, tilt-test, and 24 hour Holter recording (performed if clinically indicated), and able to provide informed consent. Exclusion Criteria: Syncope caused by structural heart disease.	% patients with change in disease management: ILR: 41.7 Conventional: 7.1 p-value: <0.001 --- Specific changes in management (number of patients): ILR: Pacemaker 16, Lifestyle change 12 Drug therapy 8, Drug cessation 2 RF ablation 1, Awaiting therapy 2 Tilt training 1, Psychiatry referral 1 Conventional: Pacemakers 3, Drug therapy 1 ICD 1, Drug cessation 1 Lifestyle change 1 --- % patients with second syncope recurrence: ILR: 15.5 Conventional: 23.5 p-value: 0.21 --- Time to second syncope recurrence: p-value: 0.04 (longer for ILR group) --- % Mortality: ILR: 7.8 Conventional: 9.2 --- Quality of life: No difference in SF-12. Significant increase in VAS well-being score at 18 months in ILR group (p = 0.03).

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Brignole et al. 2006(54)	Design: Before-after study (case series) with Phase II comparison of treatment strategy Purpose: To assess the effectiveness of a diagnostic and treatment strategy, based on the initial evaluation, early ILR implantation, and ILR-based specific therapy after syncope recurrence, in patients with recurrent suspected neurally-mediated syncope. ECRI Quality Score (Rating): 6.4 (Low)	Monitor: ILR (Reveal Plus) Control: No comparison with another monitoring device. Phase II of the study divided diagnosed patients into two groups that received different treatment strategies.	Total Enrolled (Phase II only): 103 Age mean ± SD 67 ±14 % female: 57 Inclusion Criteria: Eligible patients were at least 30 years of age and had suffered, in the prior 2 years, three or more syncope episodes of suspected neurally-mediated syncope (NMS) which was considered by the attending physician to be a severe clinical presentation (because of high number of episodes that affect patient's quality of life or high risk for physical injury due to unpredictable occurrence) requiring treatment initiation. Exclusion Criteria: Patients with induced carotid sinus syncope were excluded.	% patients with syncope recurrence: ILR-based specific therapy: 11.3 No specific therapy: 34 p-value: 0.009 % patients with presyncope: ILR-based specific therapy: 7.5 No specific therapy: 16 p-value: 0.23

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Deharo et al. 2006(55)	Design: Before-after study (case series) Purpose: To analyze the heart rhythm during spontaneous vasovagal syncope in highly symptomatic patients with ILRs and to correlate this rhythm with the heart rhythm observed during head-up tilt test. ECRI Quality Score (Rating): 8.4 (Moderate)	Monitor: ILR (Reveal or Reveal Plus) Control: None	Total Enrolled: 25 Age mean (range) 60.2 ±17.1 years % female: 56 Inclusion Criteria: Consecutive patients presenting with a history of recurrent syncope were included if they met the following criteria: 1) diagnosis of vasovagal syncope established on the basis of history, physical examination, carotid sinus massage, 12-lead ECG, and a positive HUT either at baseline or after drug provocation (additional tests were performed for differential diagnosis when needed); 2) a history of frequent syncope severely impairing quality of life (i.e., more than three episodes in the previous two years with an interval between the first and second episode of more than six months); 3) the absence of heart disease and cardiovascular treatment; and 4) signed informed consent. Exclusion Criteria: Heart disease and cardiovascular treatment.	% patients with change in disease management: 28 --- Specific changes in management (number of patients): Drug therapy 4 Pacemaker 3
Inamdar et al. 2006(9)	Design: Before-after study (case series) Purpose: to review the authors' 5-year experience with ILRs in identifying the etiology of recurrent syncope. ECRI Quality Score (Rating): 5.9 (Low)	Monitor: ILR (Reveal or Reveal Plus) Control: None	Total Enrolled: 100 Age mean (range) 68 ±18 years % female: 30 Inclusion Criteria: Patients with syncope or presyncope of unknown etiology (who had a negative tilt table test, electrophysiologic study and neurologic workup) monitored with Reveal or Reveal Plus. Exclusion Criteria: None	% patients with change in disease management: 45 --- Specific changes in management (number of patients): Pacemaker 27 Drug therapy 7 ICD 6 AV junction ablation 4 AV junction ablation + pacemaker 1

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Brignole et al. 2005(56)	Design: Before-after study Purpose: To evaluate the usage and diagnostic yield of the ILR in detection of the mechanism of syncope and in guiding therapy in patients aged ≥65 years and comparing them with those <65 years. ECRI Quality Score (Rating): 8.4 (Moderate)	Monitor: ILR (Reveal and Reveal Plus) Control: None	Total Enrolled: 103 Age mean (range) 69 ±11 years % female: 44.7 Inclusion Criteria: Consecutive patients who had both severe (high risk or high frequency) syncope that justified the need for a precise diagnosis and specific therapy and a negative work-up. High risk or high frequency syncope was defined as: 1) very frequent, with reduced quality of life or 2) were recurrent and unpredictable (absence of premonitory symptoms) thus exposing patients to "high risk" of trauma; or 3) occurred during the prosecution of a "high risk" activity (e.g., driving, machine operator, flying, competitive athletics, etc.). Exclusion Criteria: Patients were informed that ILR implantation could result in non-pharmacological therapy, e.g., pacemaker insertion, and these devices were not given to patients who were not willing to accept the eventual therapeutic recommendations.	% patients with change in disease management: 36.9 --- Specific changes in management (number of patients): Pacemaker 28 ICD 1 Catheter ablation 1 Other (drugs, bypass graft) 8 --- % Mortality: 3.9

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Lombardi et al. 2004(57)	Design: Before-after study (case series) Purpose: To facilitate the understanding of the etiology of syncope in a group of consecutive subjects with a negative cardiac and neurological workup. ECRI Quality Score (Rating): 8.0 (Moderate)	Monitor: ILR (Reveal Plus) Control: None	Total Enrolled: 34 Age mean (range) 60 ±15 years % female: 39.3 Inclusion Criteria: Consecutive patients with at least two unexplained syncopal episodes within 1 year of observation and negative neurological and cardiovascular work-up. Exclusion Criteria: Cardiac diagnosis based on medical history and physical examination, on two-dimensional echocardiogram, on detection of syncope related arrhythmias or conduction defects during Holter or telemetry monitoring and on a positive normal or nitroglycerine potentiated tilt test. Subjects with a neurological etiology of transient loss of consciousness according to medical history and physical examination, brain CT scan or nuclear magnetic resonance, baseline or sleep deprived electroencephalogram were also excluded.	% patients with change in disease management: 32.4 --- Specific changes in management (number of patients): Pacemaker (dual) 6 Pacemaker (single) 2 RF ablation 1 ICD 1 Anti-epileptic drugs 2

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Krahn et al. 2004(58)	Design: Before-after study (case series) Purpose: To determine whether detection of significant asymptomatic arrhythmias would facilitate diagnosis in patients with unexplained syncope ECRI Quality Score (Rating): 8.0 (Moderate)	Monitor: ILR (Reveal Plus) Control: None	Total Enrolled: 60 Age mean (range) 67 ±16 years % female: 55 Inclusion Criteria: Consecutive patients referred for investigation of syncope with a left ventricular ejection fraction ≥35%. Patients had recurrent unexplained syncope or a single episode associated with physical injury that warranted cardiovascular investigation. Conventional testing, such as tilt test and Holter monitoring, were unable to provide a diagnosis for the syncopal episodes. Exclusion Criteria: Patients were excluded when the left ventricular ejection fraction was <35%, when they were unlikely to survive for 1 year, and when they were unable to provide follow-up or give informed consent. Patients with a presentation typical of neurally mediated syncope at baseline assessment were considered to have this diagnosis and were excluded. This included upright posture with a prodrome including warmth and diaphoresis, with post-episode fatigue.	% patients with change in disease management: 35 --- Specific changes in management (number of patients): Pacemaker 17 Ablation 2 Drug therapy 2

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Armstrong et al. 2003(59)	Design: Before-after study (case series) Purpose: To present the authors' experience with the Reveal ILR in older subjects referred to a dedicated falls and syncope clinic in whom usual clinical assessment had not satisfactorily identified an attributable diagnosis but where a cardiovascular cause for syncope or falls was suspected. ECRI Quality Score (Rating): 6.8 (Low)	Monitor: Reveal ILR Control: None	Total Enrolled: 15 Age mean (range) 73 (61 to 89) years % female: 86.7 Inclusion Criteria: Consecutive patients over 60 years of age with syncope, unexplained falls or both conditions. Exclusion Criteria: None	% patients with change in disease management: 20 --- Specific changes in management (number of patients): Pacemaker (dual-chamber) 3
Ermis et al. 2003(60)	Design: Before-after study (case series) Purpose: To evaluate the diagnostic utility of the auto-trigger ILR recording mode in patients evaluated for syncope. ECRI Quality Score (Rating): 7.7 (Moderate)	Monitor: ILR (Reveal Plus) Control: None	Total Enrolled: 50 Age mean (range) 64.2 ±21.5 years % female: 46 Inclusion Criteria: Consecutive patients with >2 syncopal episodes within the year before implant, or had experienced a significant physical injury with a syncope event. Exclusion Criteria: None	% patients with change in disease management: 32 --- Specific changes in management (number of patients): Pacemaker 10 RF ablation 4 ICD 2

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Krahn et al. 2001(62)	Design: Before-after study (case series) Purpose: To assess the diagnostic value of recording the cardiac rhythm during presyncope in patients undergoing monitoring for undiagnosed syncope. ECRI Quality Score (Rating): 8.4 (Moderate)	Monitor: Reveal ILR Control: None	Total Enrolled: 85 Age mean (range) 59 ±18 years % female: 48.2 Inclusion Criteria: Consecutive patients with unexplained syncope after a history, physical examination, electrocardiogram, and ≥24 hours of ambulatory or in-hospital monitoring. Patients were eligible if they had ≥2 syncopal episodes within the previous 12 months or a single episode with a history of multiple presyncopal episodes. Syncope was defined as a transient loss of consciousness with spontaneous recovery, not requiring carioversion or defibrillation. Presyncope was defined as a transient alteration in level of consciousness without loss of consciousness. This encompassed episodes described by the patient as near loss of consciousness, dizziness, lightheadedness, weak spells, and feeling faint. Exclusion Criteria: Patients were excluded if they were unlikely to survive 1 year, were unable to give informed consent, had a previous implanted programmable medical device, were pregnant, or were female of childbearing age and not using a reliable form of contraception.	% patients with change in disease management: 15.3 --- Specific changes in management (number of patients): Pacemaker 13 --- % Mortality: 2.9

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Nierop et al. 2000(63)	Design: Before-after study (case series) Purpose: To assess the feasibility of recording the cardiac rhythm during syncope in patients with unexplained recurrent syncope and to describe the ECG findings. ECRI Quality Score (Rating): 9.3 (Moderate)	Monitor: Reveal ILR Control: None	Total Enrolled: 35 Age mean (range) 65 ±17 years % female: 57.1 Inclusion Criteria: Consecutive patients with two or more witnessed episodes of syncope of unknown origin within the previous 12 months or one episode with significant trauma. Exclusion Criteria: Previous MI with ejection fractions <0.40, dilated or hypertropic cardiomyopathy, nonsustained ventricular tachycardia of more than 16 beats on the Holter recording, aortic valve disease, significant left ventricular outflow obstructions on the echocardiogram, proven orthostatic hypotension, explicit vasovagal syncope, and hypersensitive cartoid sinus syndrome. Elderly patients (>80) using more than three cardioactive drugs and patients with dementia or Alzheimer's disease were also excluded.	% patients with change in disease management: 22.9 --- Specific changes in management (number of patients): Pacemaker 4 RF ablation 2 Antiarrhythmic drugs 2 --- Mean syncope rate: 1 year before ILR: 4.8 ±2.4 1 year after ILR: 1.3 ±0.7 Note: these numbers only represent the 17/35 patients who had at least 1 year of followup. --- % Mortality: 8.6
Krahn et al. 1998(64)	Design: Before-after study (case series) Purpose: To use an ILR to establish cardiac rhythm during spontaneous syncope in patients with negative ambulatory monitoring, tilt table and electrophysiological testing. ECRI Quality Score (Rating): 9.3 (Moderate)	Monitor: Prototype of Reveal ILR Control: None	Total Enrolled: 24 Age mean (range) 59 ±17 years % female: 29.2 Inclusion Criteria: All patients referred for evaluation of syncope who agreed to participate and who remained undiagnosed after clinical assessment, ambulatory or inpatient monitoring, myocardial imaging, tilt and electrophysiologic testing who were referred for evaluation of syncope. Exclusion Criteria: None	% patients with change in disease management: 75 --- Specific changes in management (number of patients): Pacemaker 8 Beta-blockers 6 Pacemaker correction 1 RF ablation 1 Antiarrhythmic therapy 1 Counseling 1

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Studies of external loop recorders (ELR)				
Jabaudon et al. 2004(65)	Design: Before-after study (case series) Purpose: To test the hypothesis that 7-day ambulatory ECG monitoring using an ELR would detect otherwise occult episodes of atrial fibrillation and flutter after acute stroke or transient ischemic attack (TIA). ECRI Quality Score (Rating): 7.7 (Moderate)	Monitor: ELR (R Test Evolution II) Control: None	Total Enrolled: 132 Age mean (range) Range (37 to 93) % female: 32.2 Inclusion Criteria: Consecutive patients with a suspicion of acute stroke or TIA were systematically screened for embolic arrhythmias using standard ECG. In the absence of AF on standard ECG, patients underwent 24-hour ECG recording (Holter), followed by ambulatory monitoring by an ELR in patients with a normal Holter. Exclusion Criteria: Patients with previously documented persistent AF, with recent (<12 months) AF paroxysm, with primarily hemorrhagic stroke, or with acute large vessel dissection were excluded.	% patients with change in disease management: 3.8 --- Specific changes in management (number of patients): Oral anticoagulation therapy 5 --- % Mortality: 0.7
Studies of post-event recorders				
Kinlay et al. 1996(12)	Design: Randomized crossover trial Purpose: To compare the diagnostic yield and cost-effectiveness of transtelephonic even monitors with those of Holter monitoring in patients with intermittent palpitations. ECRI Quality Score (Rating): 7.5 (Moderate)	Monitor: Post-event monitor (models not reported) Control: Holter monitor	Total Enrolled: 45 Age mean (range) 45 ±19 years % female: 88 Inclusion Criteria: All patients with palpitations referred to the cardiovascular unit for Holter monitoring who did not have any exclusion criteria. Exclusion Criteria: Patients being monitored for silent ischemia, assessment of therapy, syncope, or other research studies or inpatient monitoring; patients considered too old, too feeble, or too young to use the event monitor, and patients who had previously had Holter monitoring for their symptoms.	% patients with change in disease management: Post-event monitor: 18 Holter monitor: 0 --- Specific changes in management (number of patients): Not reported

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Studies of real-time continuous attended monitors				
Rothman et al. 2007(11)	Design: Randomized controlled trial Purpose: To compare the relative value of a mobile cardiac outpatient telemetry system (MCOT) with a patient-activated ELR for symptoms thought to be due to an arrhythmia ECRI Quality Score (Rating): 8.0 (Moderate)	Monitor: MCOT Control: ELR (different models)	Total Enrolled: 305 Age mean (range) MCOT: 57 ±16 years ELR: 55 ±16 years % female: MCOT: 62.7 ELR: 69.9 Inclusion Criteria: Patients with: a) a high clinical suspicion of a malignant arrhythmia, b) symptoms of syncope, presyncope, or severe palpitations occurring less frequently than once per 24 hours, and c) a nondiagnostic 24 hour Holter or telemetry monitor within 45 days prior to enrollment. Exclusion Criteria: Patients with NYHA Class IV heart failure, myocardial infarction within the prior three months, unstable angina, candidate for or recent valvular cardiac surgery, history of sustanined ventricular tachycardia or ventricular fibrillation, complex ectopy defined as ventricular premature depolarizations (VPDs) ≥10/hour with a documented ejection fraction ≤35%, subjects <18 years of age, and a concomitant condition prohibiting completion of or complicance with the protocol.	% patients with change in disease management: MCOT: 41.4 ELR: 14.6 --- Specific changes in management (number of patients): Not reported

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Studies tabled but not analyzed				
Schickendantz et al. 2006(48)	Design: Before-after study (case series) Purpose: To report the authors' initial experience with a wireless Holter system in pediatric patients with suspected dysrhythmias. ECRI Quality Score (Rating): Not rated	Monitor: Telemetric Holter system Control: None	Total Enrolled: 37 Age median (range) 8.4 (0.1 to 22) years % female: 45.9 Inclusion Criteria: Pediatric patients with a history of possible dysrhythmias. Exclusion Criteria: None	% patients with change in disease management: 35.1 --- Specific changes in management (number of patients): RF ablation 5 Drug therapy initiated or intensified 5 Psychiatric referrals 2 ICD plus drug therapy 1
Joshi et al. 2005(49)	Design: Before-after study (case series) Purpose: Assess the results of the first 100 patients monitored by the Cardionet system. ECRI Quality Score (Rating): 6.8 (Low)	Monitor: CardioNet system Control: None	Total Enrolled: 100 Age mean (range) 55 (17 to 92) % female: 52 Inclusion Criteria: All of the first 100 patients monitored by CardioNet Exclusion Criteria: None	% patients with change in disease management: 34 --- Specific changes in management: Start drug treatment 14 Permanent pacemaker 5 Ablation 4 Change drug treatment 3 ICD insertion 2 Stop anticoagulation 2 Alternate diagnosis mode 2 Pacemaker replacement 1 Stop drug treatment 1
Shimetani et al. 2005(50)	Design: Before-after study (case series) Purpose: To assess the clinical value of a real-time ECG system in aiding diagnosis and management of patients with subjective thoracic-related symptoms. ECRI Quality Score (Rating): Not rated	Monitor: Real-time event recorder Control: None	Total Enrolled: 30 Age mean (range) 61 (31 to 77) % female: 43.3 Inclusion Criteria: Patients with thorax-related complaints and an established diagnosis of either hyperlipidaemia or diabetes. Exclusion Criteria: None	% patients with change in disease management: 23.3 --- Specific changes in management (number of patients): Antiarrhythmic drug therapy 7

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Meeting abstracts				
Serwer et al. 2006(51)	Design: Before-after study (case series) Purpose: To evaluate the utility of a new system for real-time electrograms in patients with telephonic followup of pacemakers. ECRI Quality Score (Rating): Not rated	Monitor: Transtelephonic pacemaker monitoring Control: None	Total Enrolled: 114 Age median (range) 13.2 years (20 days to 54 years) % female: NR Inclusion Criteria: Patients with Medtronic Kappa 700, 900, EnPulse E1 and E2 devices Exclusion Criteria: Patients with only cell phone availability, having other devices or followed by other centers.	% patients with change in disease management: 18.4 --- Specific changes in management (number of patients): Pacemaker programming changes 21
Stellbrink et al. 2004(52)	Design: Before-after study (case series) Purpose: To evaluate the technical feasibility and clinical utility of home monitoring technology in patients with pacemakers. ECRI Quality Score (Rating): Not rated	Monitor: Home monitoring pacemaker Control: None	Total Enrolled: 122 Age mean (range) NR % female: NR Inclusion Criteria: NR Exclusion Criteria: NR	% patients with change in disease management: 17.2 --- Specific changes in management (number of patients): Proposed measures: Pacemaker reprogramming 12 Medication change 8

Table D-3. Summary of Included Studies (Key Question 4)

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Giada et al. 2007(53) Note: the two arms of this study were analyzed separately to address Key Question 3. To avoid redundancy, the data is not included in Table D-2.	Design: Randomized controlled trial Purpose: To compare the diagnostic yield and costs of ILR with those of the conventional strategy. ECRI Quality Score (Rating): 7.0 (Moderate)	Monitor: Reveal Plus ILR Control: ELR (type not specified, but appears to be patient-activated) + electrophysiological testing	Total Enrolled: 50 Age mean ± SD ILR: 51 ±18 ELR: 43 ±17 % female: ILR: 54 ELR: 79 Inclusion Criteria: Consecutive patients referred for palpitations as their chief complaint underwent an initial evaluation including history, physical examination, and ECG. Patients were enrolled if they had a negative initial evaluation, no apparent or only mild heart disease (ejection fraction >35%), and sustained (>1 min), infrequent (≤1 episode/month), and clinically significant (associated to presyncope, diaphoresis, chest pain, and asthenia) palpitations. Exclusion Criteria: Subjects with severe structural heart disease (SHD) or hereditary arrhythmogenic syndrome were excluded, as were patients with palpitations of noncardiac origin (extrasystolic or anxiety-based).	% patients with change in disease management: ILR: 73 ELR: 8.3 (excluding electrophys testing diagnoses) --- Specific changes in management (number of patients): ILR: Pacemaker 3 Antiarrhythmic drugs 8 Ablation 4 Anxiolytic therapy 4 ELR: Ablation 1 Antiarrhythmic therapy 1

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Krahn et al. 2001(61) Note: the two arms of this study were analyzed separately to address Key Question 3. To avoid redundancy, the data is not included in Table D-2.	Design: Randomized controlled trial Purpose: To determine the merit of prolonged monitoring with ILR compared to short-term testing as an initial strategy in patients with unexplained syncope. ECRI Quality Score (Rating): 7.8 (Moderate)	Monitor: Reveal Plus ILR Control: ELR + tilt table + electrophysiological testing	Total Enrolled: 60 Age mean (range) 66 ±14 years % female: 45 Inclusion Criteria: Patients with recurrent unexplained syncope or a single episode of syncope associated with injury that warranted cardiovascular investigation. Syncope must have remained unexplained after clinical assessment including postural blood pressure testing, a minimum of 24 hours of baseline ambulatory monitoring or inpatient telemetry, and a transthoracic echocardiogram. Exclusion Criteria: Patients were excluded if the left ventricular ejection fraction was <35%, if they were unlikely to survive for 1 year, or if they were unable to provide follow-up or give informed consent. Patients with a presentation typical of neurally-mediated syncope at baseline assessment were considered to have this diagnosis and were excluded. This included upright posture with a prodrome including warmth and diaphoresis, with postepisode fatigue.	% patients with change in disease management: ILR: 46.7 ELR: 3.3 (excluding tilt table and electrophys testing diagnoses) --- Specific changes in management (number of patients): ILR: Pacemaker 10 Antiarrhythmic drugs 1 Dietary interventions 3 ELR: Pacemaker 1 --- % patients with resolution of syncope: ILR: 43.3 ELR: 20

Author/Year	Study Design/Purpose	Monitor/Outcomes	Demographics	Results
Rothman et al. 2007(11)	Design: Randomized controlled trial Purpose: To compare the relative value of a mobile cardiac outpatient telemetry system (MCOT) with a patient-activated ELR for symptoms thought to be due to an arrhythmia ECRI Quality Score (Rating): 8.0 (Moderate)	Monitor: MCOT Control: ELR (different models)	Total Enrolled: 305 Age mean (range) MCOT: 57 ±16 years ELR: 55 ±16 years % female: MCOT: 62.7 ELR: 69.9 Inclusion Criteria: Patients with: a) a high clinical suspicion of a malignant arrhythmia, b) symptoms of syncope, presyncope, or severe palpitations occurring less frequently than once per 24 hours, and c) a nondiagnostic 24 hour Holter or telemetry monitor within 45 days prior to enrollment. Exclusion Criteria: Patients with NYHA Class IV heart failure, myocardial infarction within the prior three months, unstable angina, candidate for or recent valvular cardiac surgery, history of sustanined ventricular tachycardia or ventricular fibrillation, complex ectopy defined as ventricular premature depolarizations (VPDs) ≥10/hour with a documented ejection fraction ≤35%, subjects <18 years of age, and a concomitant condition prohibiting completion of or complicance with the protocol.	% patients with change in disease management: MCOT: 41.4 ELR: 14.6 --- Specific changes in management (number of patients): Not reported

Appendix E. Evidence Tables for Key Question 3

Table E-1. Patient Enrollment Criteria for Studies Addressing Key Question 3

Reference	Year	Inclusion Criteria	Exclusion Criteria
Studies included and analyzed			
Giada et al.(53)	2007	Consecutive patients referred for palpitations as their chief complaint underwent an initial evaluation including history, physical examination, and ECG. Patients were enrolled if they had a negative initial evaluation, no apparent or only mild heart disease (ejection fraction >35%), and sustained (>1 min), infrequent (≤1 episode/month), and clinically significant (associated to presyncope, diaphoresis, chest pain, and asthenia) palpitations.	Subjects with severe structural heart disease (SHD) or hereditary arrhythmogenic syndrome were excluded, as were patients with palpitations of noncardiac origin (extrasystolic or anxiety-based).
Brignole et al.(54)	2006	Eligible patients were at least 30 years of age and had suffered, in the prior 2 years, three or more syncope episodes of suspected neurally-mediated syncope (NMS) which was considered by the attending physician to be a severe clinical presentation (because of high number of episodes that affect patient's quality of life or high risk for physical injury due to unpredictable occurrence) requiring treatment initiation.	Patients with induced carotid sinus syncope were excluded.
Farwell et al.(10)	2006	Consectutive patients of age ≥16 years, acute syncope presentation, ≥2 unexplained syncopes in the past 12 months, no pacing indication following basic clinical workup, tilt-test, and 24 hour Holter recording (performed if clinically indicated), and able to provide informed consent.	Syncope caused by structural heart disease.

Reference	Year	Inclusion Criteria	Exclusion Criteria
Deharo et al.(55)	2006	Consecutive patients presenting with a history of recurrent syncope were included if they met the following criteria: 1) diagnosis of vasovagal syncope established on the basis of history, physical examination, carotid sinus massage, 12-lead ECG, and a positive HUT either at baseline or after drug provocation (additional tests were performed for differential diagnosis when needed); 2) a history of frequent syncope severely impairing quality of life (i.e., more than three episodes in the previous two years with an interval between the first and second episode of more than six months); 3) the absence of heart disease and cardiovascular treatment; and 4) signed informed consent. All patients monitored by Reveal or Reveal Plus.	Heart disease and cardiovascular treatment.
Inamdar et al.(9)	2006	Patients with syncope or presyncope of unknown etiology (who had a negative tilt table test, electrophysiologic study and neurologic workup) monitored with Reveal or Reveal Plus.	None
Brignole et al.(56)	2005	Consecutive patients who had both severe (high risk or high frequency) syncope that justified the need for a precise diagnosis and specific therapy and a negative work-up. High risk or high frequency syncope was defined as: 1) very frequent, with reduced quality of life or 2) were recurrent and unpredictable (absence of premonitory symptoms) thus exposing patients to “high risk” of trauma; or 3) occurred during the prosecution of a “high risk” activity (e.g., driving, machine operator, flying, competitive athletics, etc.). All patients monitored by Reveal or Reveal Plus.	Patients were informed that ILR implantation could result in non-pharmacological therapy, e.g., pacemaker insertion, and these devices were not given to patients who were not willing to accept the eventual therapeutic recommendations.
Lombardi et al.(57)	2004	Consecutive patients with at least two unexplained syncopal episodes within 1 year of observation and negative neurological and cardiovascular work-up. All patients monitored by Reveal Plus.	Cardiac diagnosis based on medical history and physical examination, on two-dimensional echocardiogram, on detection of syncope related arrhythmias or conduction defects during Holter or telemetry monitoring and on a positive normal or nitroglycerine potentiated tilt test. Subjects with a neurological etiology of transient loss of consciousness according to medical history and physical examination, brain CT scan or nuclear magnetic resonance, baseline or sleep deprived electroencephalogram were also excluded.

Reference	Year	Inclusion Criteria	Exclusion Criteria
Krahn et al.(58)	2004	Consecutive patients referred for investigation of syncope with a left ventricular ejection fraction ≥35%. Patients had recurrent unexplained syncope or a single episode associated with physical injury that warranted cardiovascular investigation. Conventional testing, such as tilt test and Holter monitoring, were unable to provide a diagnosis for the syncopal episodes. All patients monitored by Reveal Plus.	Patients were excluded when the left ventricular ejection fraction was <35%, when they were unlikely to survive for 1 year, and when they were unable to provide follow-up or give informed consent. Patients with a presentation typical of neurally mediated syncope at baseline assessment were considered to have this diagnosis and were excluded. This included upright posture with a prodrome including warmth and diaphoresis, with post-episode fatigue.
Armstrong et al.(59)	2003	Consecutive patients over 60 years of age with syncope, unexplained falls or both conditions monitored by Reveal.	None.
Ermis et al.(60)	2003	Consecutive patients with >2 syncopal episodes within the year before implant, or had experienced a significant physical injury with a syncope event. All patients monitored by Reveal Plus.	None.
Krahn et al.(62)	2001	Consecutive patients with unexplained syncope after a history, physical examination, electrocardiogram, and ≥24 hours of ambulatory or in-hospital monitoring. Patients were eligible if they had ≥2 syncopal episodes within the previous 12 months or a single episode with a history of multiple presyncopal episodes. Syncope was defined as a transient loss of consciousness with spontaneous recovery, not requiring carioversion or defibrillation. Presyncope was defined as a transient alteration in level of consciousness without loss of consciousness. This encompassed episodes described by the patient as near loss of consciousness, dizziness, lightheadedness, weak spells, and feeling faint. All patients monitored by Reveal ILR.	Patients were excluded if they were unlikely to survive 1 year, were unable to give informed consent, had a previous implanted programmable medical device, were pregnant, or were female of childbearing age and not using a reliable form of contraception.
Krahn et al.(61)	2001	Patients with recurrent unexplained syncope or a single episode of syncope associated with injury that warranted cardiovascular investigation. Syncope must have remained unexplained after clinical assessment including postural blood pressure testing, a minimum of 24 hours of baseline ambulatory monitoring or inpatient telemetry, and a transthoracic echocardiogram.	Patients were excluded if the left ventricular ejection fraction was <35%, if they were unlikely to survive for 1 year, or if they were unable to provide follow-up or give informed consent. Patients with a presentation typical of neurally-mediated syncope at baseline assessment were considered to have this diagnosis and were excluded. This included upright posture with a prodrome including warmth and diaphoresis, with postepisode fatigue.

Reference	Year	Inclusion Criteria	Exclusion Criteria
Nierop et al.(63)	2000	Consecutive patients with two or more witnessed episodes of syncope of unknown origin within the previous 12 months or one episode with significant trauma. All patients monitored by Reveal ILR.	Previous MI with ejection fractions <0.40, dilated or hypertropic cardiomyopathy, nonsustained ventricular tachycardia of more than 16 beats on the Holter recording, aortic valve disease, significant left ventricular outflow obstructions on the echocardiogram, proven orthostatic hypotension, explicit vasovagal syncope, and hypersensitive cartoid sinus syndrome. Elderly patients (>80) using more than three cardioactive drugs and patients with dementia or Alzheimer's disease were also excluded.
Krahn et al.(64)	1998	All patients referred for evaluation of syncope who agreed to participate and who remained undiagnosed after clinical assessment, ambulatory or inpatient monitoring, myocardial imaging, tilt and electrophysiologic testing who were referred for evaluation of syncope.	None.
Jabaudon et al.(65)	2004	Consecutive patients with a suspicion of acute stroke or TIA were systematically screened for emboligenic arrhythmias using standard ECG. In the absence of AF on standard ECG, patients underwent 24-hour ECG recording (Holter), followed by ambulatory monitoring by an ELR in patients with a normal Holter.	Patients with previously documented persistent AF, with recent (<12 months) AF paroxysm, with primarily hemorrhagic stroke, or with acute large vessel dissection were excluded.
Kinlay et al.(12)	1996	All patients with palpitations referred to the cardiovascular unit for Holter monitoring who did not have any exclusion criteria.	Patients being monitored for silent ischemia, assessment of therapy, syncope, or other research studies or inpatient monitoring; patients considered too old, too feeble, or too young to use the event monitor, and patients who had previously had Holter monitoring for their symptoms.
Rothman et al.(11)	2007	Patients with: a) a high clinical suspicion of a malignant arrhythmia, b) symptoms of syncope, presyncope, or severe palpitations occurring less frequently than once per 24 hours, and c) a nondiagnostic 24 hour Holter or telemetry monitor within 45 days prior to enrollment.	Patients with NYHA Class IV heart failure, myocardial infarction within the prior three months, unstable angina, candidate for or recent valvular cardiac surgery, history of sustanined ventricular tachycardia or ventricular fibrillation, complex ectopy defined as ventricular premature depolarizations (VPDs) ≥10/hour with a documented ejection fraction ≤35%, subjects <18 years of age, and a concomitant condition prohibiting completion of or complicance with the protocol.

Reference	Year	Inclusion Criteria	Exclusion Criteria
Studies tabled but not analyzed			
Schickendantz et al.(48)	2006	Pediatric patients with a history of possible dysrhythmias.	None
Joshi et al.(49)	2005	All of the first 100 patients monitored by CardioNet.	None
Shimetani et al.(50)	2005	Patients with thorax-related complaints and an established diagnosis of either hyperlipidaemia or diabetes. All patients monitored with Event Recorder.	None
Meeting abstracts			
Serwer et al.(51)	2006	Patients with Medtronic Kappa 700, 900, EnPulse E1 and E2 devices	Patients with only cell phone availability, having other devices or followed by other centers.
Stellbrink et al.(52)	2004	NR	NR

NR – Not reported.

Table E-2. Characteristics of Patients Receiving Remote Cardiac Monitoring

Author/ year	Year	Monitoring device	N	Age	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease	% patients with normal baseline ECG
Studies included and analyzed										
Giada et al.(53)	2007	ILR	26	51 ±18	54	Palpitations (suspected to be cardiac-related)	44 (15-100)	42	Structural heart disease (valvular heart disease, ischemic heart disease, dilated cardiomyopathy)	NR
		Conventional	24	43 ±17	79		30 (15-66) Median and IQ range, months	25		NR
Brignole et al.(54)	2006	ILR	103	67 ±14	57	Syncope (suspected to be neurally-mediated) (100%)	6 (4-13) Median and IQ range, years	12%	Structural heart disease	87
Farwell et al.(10)	2006	ILR	103	73.9 (61.6 to 80.7)	55.3	Syncope (100%)	12 (6 to 36)	47.6	Ischemic, other types NR	NR
		Conventional	98	74.1 (59.1 to 81.0) Median and IQ range	53.1		18 (5 to 48)	52.0		

Author/ year	Year	Monitoring device	N	Age	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease	% patients with normal baseline ECG
Deharo et al.(55)	2006	ILR	25	60.2 ±17.1	56	Syncope (100%)	7.7 ±14.1 years	0	NA	NR
Inamdar et al.(9)	2006	ILR	100	68 ±18	70	Syncope or presyncope – no info on % of each	NR	45	Coronary artery disease, dilated cardiomyopathy, valvular defects, atrial fibrillation, MI	100
Brignole et al.(56)	2005	ILR	103	69 ±11	44.6	Syncope (100%)	NR	38	MI, dilated cardiomyopathy, valvular heart disease	NR
Lombardi et al.(57)	2005	ILR	34	60 ±15	38.3	Syncope (100%)	NR	20.6	Carotid or peripheral atherosclerosis, dilated cardimyopathy, mild aortic stenosis	NR
Krahn et al.(58)	2004	ILR	60	67 ±16	55	Syncope (100%)	10.8 months	42	MI, angina/CABG, cardiomyopathy, vulvular heart disease, moderate or greater valvular lesion or previous valve surgery	NR

Author/ year	Year	Monitoring device	N	Age	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease	% patients with normal baseline ECG
Armstrong et al.(59)	2003	ILR	15	73 (61-89)	86.7	Syncope (40%) Unexplained falls (20%) Syncope and unexplained falls (40%)	48 months (4-200)	53.3	Ischaemic heart disease, cerebrovascular disease	66.7
Ermis et al.(60)	2003	ILR	50	64 ±22	46	Syncope (100%)	NR	18	Coronary artery disease, dilated cardiomyopathy, atrial septal defect	NR
Krahn et al.(61)	2001	ILR	85	59 ±18	48.2	Syncope (100%)	5.5 ±8.9 years	62	Angina, MI, previous cardiac arrest, cardiomyopathy, cardiomegaly, congestive heart failure, and valvular, congenital or pericardial heart disease	NR

Author/ year	Year	Monitoring device	N	Age	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease	% patients with normal baseline ECG
Krahn et al.(61)	2001	ILR ELR	30 30	68 ±14 64 ±14	37 53	Syncope (100%)	6.6 ±12.1 8.7 ±26.6	43 33	Ischemic heart disease ILR: 30 ELR: 17 Valvular heart disease: ILR: 3 ELR: 17 Cardiomyopathy: ILR: 10 ELR: 0	67 73
Nierop et al.(63)	2000	ILR	35	65 (29-87)	57	Syncope (100%)	NR	8.6	MI, hypertropic cardiomyopathy	54
Krahn et al.(64)	1998	Prototype of ILR (reveal)	24	59 ±17	29	Syncope (100%)	NR	45.8	Coronary artery disease, hypertension, previous cardiac transplant, hypertrophic cardiomyopathy, 1 mitral stenosis	NR

Author/ year	Year	Monitoring device	N	Age	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease	% patients with normal baseline ECG
Jabaudon et al.(65)	2004	ELR	149	66 (37 to 93) in non-AF patients; 72 (56-91) in AF patients (N = 22)	32.2	Acute stroke or TIA	NR	16.8	NR	97.3
Kinlay et al.(12)	1996	Post-event monitor	45	45 ±19	88	Palpitations (100%)	NR	8.9	Ischemic (8.9)	NR
Rothman et al.(11)	2007	Real-time continuous attended (MCOT) ELR	134 132	57 ±16 55 ±16	62.7 68.9	Presyncope (37%) Syncope (17%) Palpitations (78%) Presyncope (31%) Syncope (15%) Palpitations (84%)	NR	84.3 82.6	Coronary artery disease, hypertension, previous MI, congestive heart failure, pacemaker	NR

Author/ year	Year	Monitoring device	N	Age	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease	% patients with normal baseline ECG
Studies tabled but not analyzed										
Schickendantz et al.(48)	2006	Wireless digital Holter	37	8.4 (.1 to 22)	45.9	Dysrhythmias	NR	NR	NR	NR
Joshi et al.(49)	2005	Real-time continuous attended (MCOT)	100	55 (range 17 to 92)	52	Palpitations (47%) Check efficacy of drugs (25%) Dizziness (24%) Syncope (19%) Monitor for ventricular tachycardia (11%) Monitor during drug initiation (8%) Check efficacy of ablation (6%) Check pacemaker function (2%) Monitor for atrial fibrillation, off treatment (1%)	NR	NR	NR	49

Author/ year	Year	Monitoring device	N	Age	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease	% patients with normal baseline ECG
Shimetani et al.(50)	2005	Real-time event monitor attended	30	61 (range 31 to 77)	43.3	Palpitations (53%) Palpitations and dizziness (17%) Thoracic discomfort (17%) Palpitations and thoracic discomfort (13%)	NR	NR	NR	NR
Meeting abstracts										
Serwer et al.(51)	2006	Pacemakers (Medtronic Kappa 700, 900, EnPulse E1 and E2)	114	13.2 years (range 20 days to 54 years)	NR	NR	NR	NR	NR	NR
Stellbrink et al.(52)	2004	Home-Monitoring pacemaker	122	NR	NR	NR	NR	NR	NR	NR

CVP – Central Venous Pressure Monitoring
EDM – Esophageal Doppler Monitoring
IQR – Interquartile Range
NR – Not reported.

Table E-3. Study Quality Evaluation – Controlled Trials Evaluating Insertable Loop Recorders

ECRI study quality scale – questions	Farwell et al. (2006)		Brignole et al. (2006)
	Mortality, syncope reduction	Change in Disease management, Quality of life	Syncope reduction
1. Were patients randomly assigned to groups?	Yes	Yes	No
2. Did the study emply stochastic randomization?	Yes	Yes	No
3. Were any methods used to make the groups comparable- randomization, matching, etc.?	Yes	Yes	No
4. Were patients assigned to groups based on factors other than patient or physician preference?	Yes	Yes	No
5. Were the characteristics of the patients in different groups comparable?	Yes	Yes	No
6. Did the patients in the different study groups have similar levels of performance on outcomes at baseline?	Yes	Yes	Yes
7. Was the study prospectively planned?	Yes	Yes	Yes
8. Did 85% or more of the patients complete the study?	Yes	Yes	Yes
9. Was there a less than 16% difference in completion rates in the study's groups?	Yes	Yes	Yes
10. Were all of the study's groups concurrently treated?	Yes	Yes	Yes
11. Was compliance with treatment greater than or equal to 85% in both of the groups?	Yes	Yes	Yes
12. Were both groups treated at the same centers?	Yes	Yes	Yes
13. Were subjects blinded to treatment?	Yes[a]	Yes[a]	Yes[a]
14. Did the authors test and confirm that blinding of patients was maintained?	Yes[a]	Yes[a]	Yes[a]
15. Was the treating physician blinded to group assignment?	No	No	No
16. Were the outcome assessors blinded to group assignment?	NR	NR	No
17. Was there concealment of allocation?	Yes	Yes	No
18. Was the outcome of interest objective and was it objectively measured?	Yes	No	Yes

ECRI study quality scale – questions	Farwell et al. (2006)		Brignole et al. (2006)
	Mortality, syncope reduction	Change in Disease management, Quality of life	Syncope reduction
19. Were the same methods used to measure outcomes in all of the study's groups?	Yes	Yes	Yes
20. Was the instrument used to measure the outcome standard?[a]	Yes	Yes	Yes
21. Was the same treatment given to all of the patients enrolled in the experimental group?	Yes	Yes	Yes
22. Was the same treatment given to all of the patients enrolled in the control group?	Yes	Yes	Yes
23. Were the follow-up times in all of the study's relevant groups approximately equal?	Yes	Yes	Yes
24. Was the funding for this study derived from a source that does not have a financial interest in its results?	No	No	No
25. Were the author's conclusions supported by the data in the *Results* section?	Yes	Yes	Yes
Quality score	8.9	8.5	6.4
Quality rating	High	High	Low

[a] For this technology, blinding of patients is unlikely to influence change in disease management or clinical outcomes. Therefore, questions 13 and 14 receive an automatic "Yes" for this question even when studies did not blind patients.

Table E-4. Study Quality Evaluation – Case Series Evaluating Insertable Loop Recorders – Change in Disease Management

ECRI study quality scale - questions	Study											
	Giada (2007)	Deharo (2006)	Inamdar (2006)	Brignole (2005)	Lombardi (2005)	Krahn (2004)	Armstrong (2003)	Ermis (2003)	Krahn (2001)	Krahn (2001)[A]	Nierop (2000)	Krahn (1998)
1. Was the study prospectively planned?	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
2. Did the study enroll all patients or consecutive patients?	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
3. Inclusion/exclusion criteria based on objective lab or clinical findings?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Inclusion/exclusion criteria established *a priori*?	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the same initial treatment given to all patients enrolled?	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Did all patients receive the same subsequent treatments?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Was the outcome measure objective and objectively measured?	No	No	No	No	No	No	No	No	No	No	No	No

ECRI study quality scale - questions	Study											
	Giada (2007)	Deharo (2006)	Inamdar (2006)	Brignole (2005)	Lombardi (2005)	Krahn (2004)	Armstrong (2003)	Ermis (2003)	Krahn (2001)	Krahn (2001)[A]	Nierop (2000)	Krahn (1998)
8. Did 85% or more of the patients complete the study?	Yes	Yes	Yes	Yes	NR	NR	No	No	Yes	Yes	Yes	Yes
9. Were characteristics of those who did not complete the study similar to those who did not complete the study?	Yes	Yes	Yes	Yes	NR	NR	NR	NR	Yes	Yes	Yes	Yes
10. Was the funding for this study derived from a source that does not have a financial interest in its results?	No	NR	No	NR	NR	NR	NR	NR	NR	Yes	NR	NR
11. Were the author's conclusions supported by the data in the results section?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Quality score	8.2	7.5	5.0	7.5	7.0	7.0	5.9	6.8	7.5	9.1	8.4	8.4
Quality rating	Moderate	Moderate	Low	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate	Moderate

[a] Single arm from RCT

Table E-5. Study Quality Evaluation – Studies of External Loop Recorders and Post-Event Recorders– Change in Disease Management

ECRI study quality scale - questions	ELR Giada (2007)	ELR Rothman (2007)	ELR Jabaudon (2004)	ELR Krahn (2001)	Post-event Kinlay (1996)
1. Was the study prospectively planned?	Yes	Yes	Yes	Yes	Yes
2. Did the study enroll all patients or consecutive patients?	Yes	Yes	Yes	Yes	No
3. Inclusion/exclusion criteria based on objective lab or clinical findings?	Yes	Yes	Yes	Yes	Yes
4. Inclusion/exclusion criteria established *a priori*?	Yes	Yes	Yes	Yes	Yes
5. Was the same initial treatment given to all patients enrolled?	Yes	Yes	Yes	Yes	Yes
6. Did all patients receive the same subsequent treatments?	Yes	Yes	Yes	Yes	Yes
7. Was the outcome measure objective and objectively measured?	No	No	No	No	No
8. Did 85% or more of the patients complete the study?	Yes	Yes	No	Yes	Yes
9. Were characteristics of those who did not complete the study similar to those who did not complete the study?	Yes	Yes	NR	Yes	Yes
10. Was the funding for this study derived from a source that does not have a financial interest in its results?	No	No	NR	Yes	NR
11. Were the author's conclusions supported by the data in the *Results* section?	Yes	Yes	Yes	Yes	Yes
Quality score	8.2	8.2	6.8	9.1	7.5
Quality rating	Moderate	Moderate	Low	Moderate	Moderate

Table E-6. Study Quality Evaluation – Controlled Trials of Real-Time Continuous Attended Monitors

ECRI study quality scale – questions	Rothman et al. Change in Disease management
1. Were patients randomly assigned to groups?	Yes
2. Did the study emply stochastic randomization?	Yes
3. Were any methods used to make the groups comparable- randomization, matching, etc.?	Yes
4. Were patients assigned to groups based on factors other than patient or physician preference?	Yes
5. Were the characteristics of the patients in different groups comparable?	Yes
6. Did the patients in the different study groups have similar levels of performance on outcomes at baseline?	Yes
7. Was the study prospectively planned?	Yes
8. Did 85% or more of the patients complete the study?	Yes
9. Was there a less than 16% difference in completion rates in the study's groups?	Yes
10. Were all of the study's groups concurrently treated?	Yes
11. Was compliance with treatment greater than or equal to 85% in both of the groups?	Yes
12. Were both groups treated at the same centers?	Yes
13. Were subjects blinded to treatment?	Yes[a]
14. Did the authors test and confirm that blinding of patients was maintained?	Yes[a]
15. Was the treating physician blinded to group assignment?	No
16. Were the outcome assessors blinded to group assignment?	Yes
17. Was there concealment of allocation?	Yes
18. Was the outcome of interest objective and was it objectively measured?[a]	No
19. Were the same methods used to measure outcomes in all of the study's groups?[a]	Yes
20. Was the instrument used to measure the outcome standard?[a]	Yes
21. Was the same treatment given to all of the patients enrolled in the experimental group?	Yes

ECRI study quality scale – questions	Rothman et al.
	Change in Disease management
22. Was the same treatment given to all of the patients enrolled in the control group?	Yes
23. Were the follow-up times in all of the study's relevant groups approximately equal?	Yes
24. Was the funding for this study derived from a source that does not have a financial interest in its results?	No
25. Were the author's conclusions supported by the data in the *Results* section?	Yes
Quality score	8.8
Quality rating	High

[a] For this technology, blinding of patients is unlikely to influence change in disease management or clinical outcomes. Therefore, questions 13 and 14 receive an automatic "Yes" for this question even when studies did not blind patients.

Table E-7. Results for Key Question 3 – Change in Disease Management

Publication	N	Length of follow-up	Device	% patients receiving a diagnosis	Diagnoses	% patients with ECG-guided treatment changes	Types of treatment changes
Implantable loop recorders (ILR)							
Giada et al. 2007(53)	26	Mean: 321 ±235 days (ILR)	Reveal Plus ILR	73 (19/26)	6 SVT; 4 AF; 2 atrial flutter; 4 sinus tachycardia; 2 sinus bradycardia; 1 paroxysmal atrioventricular block	73 (19/26)	4 ablation 8 antiarrhythmic therapy 4 anxiolytic therapy 3 pacemakers
Farwell et al. 2006(10)	103	Median 17 months (IQ range 9-23)	Reveal Plus ILR	41.7 (43/103)	15 bradycardia; 2 VT; 3 SVT; 16 SR vaso-vagal; 3 SR hyperventilation; 4 SR epilepsy.	41.7 (43/103)	16 pacemakers; 12 lifestyle modification; 8 drug therapy; 2 drug cessation; 2 awaiting therapy; 1 RF ablation; 1 tilt training; 1 psychiatry reference.
			Conventional assessment	7.1 (7/98)	3 bradycardia; 1 VT; 1 SR vaso-vagal; 1 epilepsy; 1 reactive hypoglycemia	7.1 (7/98)	3 pacemakers; 1 drug therapy; 1 drug cessation; 1 ICD; 1 lifestyle modification

Publication	N	Length of follow-up	Device	% patients receiving a diagnosis	Diagnoses	% patients with ECG-guided treatment changes	Types of treatment changes
Deharo et al. 2006(55)	25	18 months for 23 patients, 2 lost to follow-up at 4 and 6 months.	Reveal ILR (3 patients); Reveal Plus ILR (22 patients)	100 (25/25)	14 general vasovagal syncope; 5 slow heart rate; 3 sinus arrest preceded by sinus bradycardia leading to an asystole; 2 severe sinus bradycardia; 1 sudden onset atrioventricular block.	28 (7/25)	4 midodrine; 3 pacemaker
Inamdar et al. 2006(9)	100	9 ±8 months	Reveal ILR (10); Reveal Plus ILR (90)	45 (45/100)	51 diagnoses (some patients had more than one) 26 bradycardia; 21 tachycardia; 2 premature atrial contraction; 1 premature ventricular contraction; 1 sick sinus syndrome.	45 (45/100)	27 pacemaker; 4 AV junction ablation, 1 AV junction ablation followed by pacemaker; 6 defibrillator implantation, 7 medical therapy
Brignole et al. 2005(56)	103	14 ±10 months	22 Reveal ILR; 81 Reveal Plus ILR	37.9 (39/103)	21 persistent/paroxysmal AV block; 13 sinus bradycardiua/sinus arrest; 3 atrial tachycardia/fibrillation; 2 ventricular tachycardia/fibrillation.	36.9 (38/103)	28 pacemaker; 1 implantable defibrillator; 1 catheter ablation; 8 other (drugs, by-pass graft)

Publication	N	Length of follow-up	Device	% patients receiving a diagnosis	Diagnoses	% patients with ECG-guided treatment changes	Types of treatment changes
Lombardi et al. 2005(57)	34	7 ±4 months (range 1-14)	Reveal Plus ILR	50 (17/34)	6 bradycardia or asystole, 3 advanced A-V block, 1 AF with wide QRS tachycardia, 2 SR epilepsy, 2 symptomatic sinus tachycardia, 1 wide QRS tachycardia, 1 postural hypotension, 1 TIA	32.4 (11/34)	2 single chamber pacemaker; 6 dual chamber pacemaker; 1 radiofrequency ablation of the slow atrioventricular nodal pathway; 1 monomorphic ventricular tachycardia was induced during electrical stimulation and a cardioverter defibrillator was implanted; 2 anti-epileptic therapy initiated.
Krahn et al. 2004(58)	60	1 year or until a diagnosis was obtained	Reveal Plus ILR	38.3 (23/60)	17 bradycardia; 6 tachycardia	35 (21/60)	17 pacemaker; 2 ablation; 2 antiarrhthmic drug therapy
Armstrong et al. 2003(59)	15	18 months or until activated by patient- no mean follow-up given	Reveal ILR	26.7 (4/15)	3 Significant bradycardias; 1 ventricular tachycardia	20 (3/15)	3 dual chamber demand pacemakers; Vtrach pt awaiting further electrophysiological testing
Ermis et al. 2003(60)	50	14.3 ±7.9 months	Reveal Plus ILR	38 (19/50)	4 supraventricular tachycardia	32 (16/50)	10 pacemakers; 2 implantable cardioverter-defibrillator; 4 radiofrequency ablation.
Krahn et al. 2001(62)	85	1 year or until diagnosis	Reveal ILR	24.7 (21/85)	30 bradycardia; 5 tachycardia	15.3 (13/85)	13 pacemaker
Krahn et al. 2001(61)	30	12 months	ILR	46.7 (14/30)	10 bradycardia, 3 vasovagal syncope, 1 narrow tachycardia	46.7 (14/30)	10 pacemakers, 1 antiarrhythmic drugs, 3 dietary interventions

Publication	N	Length of follow-up	Device	% patients receiving a diagnosis	Diagnoses	% patients with ECG-guided treatment changes	Types of treatment changes
Nierop et al. 2000(63)	35	11 ±8.3 (1-30 months, median 8)	Reveal ILR	28.6 (10/35)	4 bradycardia; 6 tachycardia	22.9 (8/35)	4 pacemaker; 2 radiofrequency ablation; 2 antiarrhthmic medication
Krahn et al. 1998(64)	24	40 ±10 months	Prototype of Reveal ILR	75 (18/24)	3 AV block; 3 bradycardia; 2 sinus arrest; 1 pacemaker malfunction; 1 SVT; 1 VT; 1 psychogenic syncope; 1 hypotrophic cardiopathy; 5 vasodepressor syncope suspected	75 (18/24)	8 pacemaker; 1 pacemaker oversensing corrected; 1 radiofrequency catheter ablation of atrioventricular node reentrant tachycardia; 1 antiarrhythmic therapy; 6 beta blockers initiated; 1 counseling
External loop recorders (ELR)							
Giada et al. 2007(53)	24	40 ±25 days	ELR (without electrophys testing) ELR + electrophys testing	8.3 (2/24) 20.8 (5/24)	1 AF 1 SVT	8.3% (2/24) 20.8 (5/24)	1 ablation 1 antiarrhythmic therapy 2 ablation 1 antiarrhythmic therapy
Rothman et al. 2007(11)	132	At least 25 days	ELR	74.2 (98/132)	NR	14.6 (19/132)	NR
Jabaudon et al. 2004(65)	132	Mean 159 hours	R-test Evolution II, ELR	3.8 (5/132)	5 atrial fibrillation	3.8 (5/132)	5 oral anticoagulation therapy initiated

Publication	N	Length of follow-up	Device	% patients receiving a diagnosis	Diagnoses	% patients with ECG-guided treatment changes	Types of treatment changes
Krahn et al. 2001(61)	30	2 to 4 weeks	ELR ELR + tilt table + electrophys testing	3.3 (1/30) 20 (6/30)	1 third degree AV block	3.3 (1/30) 13.3 (4/30)	1 pacemaker 3 pacemakers, 1 ICD
Post-event recorders							
Kinlay et al. 1996(12)	45	3 months	Post-event monitor (from Aerotel or Medtronic) Holter monitor (control)	18 (8/45) 0 (0/45)	Supraventricular tachycardia or atrial fibrillation or atrial flutter	18 (8/45)	Not reported
Remote continuous attended monitors							
Rothman et al. 2007(11)	266	At least 25 days	MCOT remote continuous attended monitor ELR	87.3 (117/134) 74.2 (98/132)	NR	41.4 (55/134) 14.6 (19/132)	NR
Studies tabled but not analyzed							
Schickendantz et al.(48)	37	Median 6.5 days (range 1 to 42)	Wireless Holter	75.7 (28/37)	NR	35.1 (13/37)	5 radiofrequency ablation, 5 drug therapy initiated or intensified, 2 pyschiatric referrals, 1 ICD plus drug therapy

Publication	N	Length of follow-up	Device	% patients receiving a diagnosis	Diagnoses	% patients with ECG-guided treatment changes	Types of treatment changes
Joshi et al. 2005(49)	100	Mean 9..9 days (range 2 to 28)	MCOT remote continuous attended monitor	All patients: 51 (51/100) Patients with prior unsuccessful Holter or event monitoring: 53.3% (16/30)	NR	All patients: 32 (32/100) Patients with prior unsuccessful Holter or event monitoring: 33.3% (10/30)	14 started drug therapy; 5 pacemaker; 4 ablation; 3 changed drug treatment; 2 implantable cardioverter-defibrillator insertion; 2 stop anti-coagulation; 1 pacemaker replaced; 1 stop drug treatment
Shimetani et al. 2005(50)	30	Up to 7 days	Real-time event recorder	NR	NR	23.3 (7/30)	7 started antiarrhythmic drug therapy
Meeting abstracts							
Serwer et al. 2006(51)	114	NR	Transtelephonic pacemaker monitoring (CareLink)	NR	NR	18.4 (21/114)	21 pacemaker programming changes
Stellbrink et al. 2004(52)	122	3 months	Home monitoring pacemaker	NR	NR	17.2 (20/116)	Proposed measures: 12 pacemaker reprogramming, 8 medication change

AV –Atrioventricular.
ICD – Implantable cardioverter/defibrillator.
NR – Not reported.
SR – Sinus rhythm.
SVT – Supraventricular tachycardia.
TIA – Transient ischemic attack.
VT – Ventricular tachycardia.

Table E-8. Results for Key Question 3 – Reduction in Syncope

Study	N	% patients with syncope recurrence		p-value[a]
		ILR	Control	
Farwell et al. 2006(10)	201	Total: 46.6 (48/103) Second recurrence: 15.5 (16/103)	Total: 37.8 (37/98) Second recurrence: 23.5 (23/98)	0.25 0.21
Study	N	Time to second syncope recurrence		p-value
		ILR	Control	
Farwell et al. 2006(10)	201	NR	NR	0.04 (favoring ILR)
Study	N	% patients with syncope recurrence		p-value
		ILR-based specific therapy	ILR – no specific therapy	
Brignole et al. 2006(54)	103	Syncope: 11.3 (6/53) Presyncope: 7.5 (4/53)	Syncope: 34 (17/50) Presyncope: 16 (8/50)	0.008[a] 0.23
Study	N	Resolution of syncope in ILR patients		p-value
Krahn et al. 2001(61)	60	13/14 primary diagnosed patients (does not report corresponding number for undiagnosed patients)		NA
Study	N	Mean syncope rate		p-value
		One year before ILR	One year after ILR	
Nierop et al. 2000(63)	35	4.8 ±2.4	1.3 ±0.7	<0.01
		Note: These numbers only represent the 17/35 patients who had at least 1 year of followup.		

[a] Calculated by ECRI Institute.

NR – Not reported.

Table E-9. Results for Key Question 3 – Mortality

Study	N	% mortality	p-value
Studies with at least 1 year of followup			
Farwell et al. 2006(10)	103 98	ILR: 7.8 (8/103) Control: 9.2 (9/98)	0.80[a]
Brignole et al. 2005(56)	103	ILR: 3.9 (4/103)	NA
Krahn et al. 2001(62)	85	ILR: 2.9 (3/103)	NA
Studies with <1 year of followup			
Nierop et al. 2000(63)	35	ILR: 8.6 (3/35)	NA
Jabaudon et al. 2004(65)	149	ELR: 0.7 (1/149)	NA

[a] Calculated by ECRI Institute.

Table E-10. Results for Key Question 3 – Quality of Life

Study	N	Measurement instruments	Follow-up times	Quality of life
Farwell et al. 2006(10)	103 98	SF-12 questionnaire and visual analogue (VAS) scales	Measured at 6,12, 18 months post-enrollment	Significant increase in VAS score for general wellbeing at 18 month time point only (p = 0.03) compared to controls; no change in SF-12 when compared with controls.

Table E-11. Results of Sensitivity Analyses for Change in Management Resulting from ILR Monitoring

Study removed	Summary odds ratio (95% CI)	p value
Qualitative robustness		
Farwell et al. 2006(10)	6.8 (4.5 to 10.3)	<0.0000001
Inamdar et al. 2006(9)	6.6 (4.4 to 9.9)	<0.0000001
Brignole et al. 2005(56)	7.0 (4.6 to 10.8)	<0.0000001
Lombardi et al. 2005(57)	7.2 (4.8 to 10.7)	<0.0000001
Krahn et al. 2004(58)	7.1 (4.7 to 10.8)	<0.0000001
Armstrong et al. 2003(59)	7.3 (5.0 to 10.7)	<0.0000001
Ermis et al. 2003(60)	7.22 (4.8 to 10.9)	<0.0000001
Krahn et al. 2001(62)	8.3 (5.7 to 12.0)	<0.0000001
Krahn et al. 2001(61)	6.9 (4.7 to 10.2)	<0.0000001
Nierop et al. 2000(63)	7.4 (5.0 to 10.9)	<0.0000001
Krahn et al. 1998(64)	6.7 (4.7 to 9.5)	<0.0000001
Cumulative meta-analysis with two most recent studies (Inamdar et al., Farwell et al.) removed	6.2 (3.9 to 9.8	<0.0000001
Original random-effects meta-analysis	7.1 (4.9 to 10.3)	<0.0000001
Random-effects meta-analysis assuming 20% baseline control rate	2.2 (1.7 to 2.9)	<0.0000001

Appendix F. Evidence Tables for Key Question 4

Table F-1. Patient Enrollment Criteria for Studies Addressing Key Question 4

Reference	Year	Inclusion Criteria	Exclusion Criteria
Giada et al.(53)	2007	Consecutive patients referred for palpitations as their chief complaint underwent an initial evaluation including history, physical examination, and ECG. Patients were enrolled if they had a negative initial evaluation, no apparent or only mild heart disease (ejection fraction >35%), and sustained (>1 min), infrequent (≤1 episode/month), and clinically significant (associated to presyncope, diaphoresis, chest pain, and asthenia) palpitations.	Subjects with severe structural heart disease (SHD) or hereditary arrhythmogenic syndrome were excluded, as were patients with palpitations of noncardiac origin (extrasystolic or anxiety-based).
Krahn et al.(61)	2001	Patients with recurrent unexplained syncope or a single episode of syncope associated with injury that warranted cardiovascular investigation. Syncope must have remained unexplained after clinical assessment including postural blood pressure testing, a minimum of 24 hours of baseline ambulatory monitoring or inpatient telemetry, and a transthoracic echocardiogram.	Patients were excluded if the left ventricular ejection fraction was <35%, if they were unlikely to survive for 1 year, or if they were unable to provide follow-up or give informed consent. Patients with a presentation typical of neurally-mediated syncope at baseline assessment were considered to have this diagnosis and were excluded. This included upright posture with a prodrome including warmth and diaphoresis, with postepisode fatigue.
Rothman et al.(11)	2007	Patients with: a) a high clinical suspicion of a malignant arrhythmia, b) symptoms of syncope, presyncope, or severe palpitations occurring less frequently than once per 24 hours, and c) a nondiagnostic 24 hour Holter or telemetry monitor within 45 days prior to enrollment.	Patients with NYHA Class IV heart failure, myocardial infarction within the prior three months, unstable angina, candidate for or recent valvular cardiac surgery, history of sustanined ventricular tachycardia or ventricular fibrillation, complex ectopy defined as ventricular premature depolarizations (VPDs) ≥10/hour with a documented ejection fraction ≤35%, subjects <18 years of age, and a concomitant condition prohibiting completion of or complicance with the protocol.

NR – Not reported.

Table F-2. Characteristics of Patients in Studies Addressing Key Question 4

Author	Year	Monitoring device	N	Age (mean ±SD)	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease (%)	% patients with normal baseline ECG
Giada et al.(53)	2007	ILR ELR	26 24	51 ±18 43 ±17	54 79	Palpitations (suspected to be cardiac-related)	44 (15-100) 30 (15-66) Median and IQ range, months	42 25	Structural heart disease (valvular heart disease, ischemic heart disease, dilated cardiomyopathy)	NR NR
Krahn et al.(61)	2001	ILR ELR	30 30	68 ±14 64 ±14	37 53	Syncope (100%)	6.6 ±12.1 8.7 ±26.6	43 33	Ischemic heart disease: ILR: 30 ELR: 17 Valvular heart disease: ILR: 3 ELR: 17 Cardiomyopathy: ILR: 10 ELR: 0	67 73

Author	Year	Monitoring device	N	Age (mean ±SD)	% female	Indications for monitoring	Duration of symptoms	% patients with heart disease	Type of heart disease (%)	% patients with normal baseline ECG
Rothman et al.(11)	2007	Real-time continuous attended (MCOT)	134	57 ±16	62.7	Presyncope (37%) Syncope (17%) Palpitations (78%)	NR	84.3	Coronary artery disease, hypertension, previous MI, congestive heart failure, pacemaker	NR
		ELR	132	55 ±16	68.9	Presyncope (31%) Syncope (15%) Palpitations (84%)		82.6		

NR – Not reported.

Table F-3. Study Quality Evaluation

ECRI study quality scale - questions	Change in disease management			Syncope reduction
	Giada (2007)	Krahn (2001)	Rothman (2007)	Krahn (2001)
1. Were patients randomly assigned to groups?	Yes	Yes	Yes	Yes
2. Did the study emply stochastic randomization?	NR	NR	Yes	NR
3. Were any methods used to make the groups comparable- randomization, matching, etc.?	Yes	Yes	Yes	Yes
4. Were patients assigned to groups based on factors other than patient or physician preference?	Yes	Yes	Yes	Yes
5. Were the characteristics of the patients in different groups comparable?	No	No	Yes	No
6. Did the patients in the different study groups have similar levels of performance on outcomes at baseline?	Yes	Yes	Yes	Yes
7. Was the study prospectively planned?	Yes	Yes	Yes	Yes
8. Did 85% or more of the patients complete the study?	Yes	Yes	Yes	Yes
9. Was there a less than 16% difference in completion rates in the study's groups?	Yes	Yes	Yes	Yes
10. Were all of the study's groups concurrently treated?	Yes	Yes	Yes	Yes
11. Was compliance with treatment greater than or equal to 85% in both of the groups?	Yes	Yes	Yes	Yes
12. Were both groups treated at the same centers?	Yes	Yes	Yes	Yes
13. Were subjects blinded to treatment?	Yes[a]	Yes[a]	Yes[a]	Yes[a]
14. Did the authors test and confirm that blinding of patients was maintained?	Yes[a]	Yes[a]	Yes[a]	Yes[a]
15. Was the treating physician blinded to group assignment?	No	No	No	No
16. Were the outcome assessors blinded to group assignment?	No	No	Yes	No
17. Was there concealment of allocation?	NR	NR	Yes	NR
18. Was the outcome of interest objective and was it objectively measured?[a]	No	No	No	Yes

ECRI study quality scale - questions	Change in disease management			Syncope reduction
	Giada (2007)	Krahn (2001)	Rothman (2007)	Krahn (2001)
19. Were the same methods used to measure outcomes in all of the study's groups?[a]	Yes	Yes	Yes	Yes
20. Was the instrument used to measure the outcome standard?	Yes	Yes	Yes	Yes
21. Was the same treatment given to all of the patients enrolled in the experimental group?	Yes	Yes	Yes	Yes
22. Was the same treatment given to all of the patients enrolled in the control group?	Yes	Yes	Yes	Yes
23. Were the follow-up times in all of the study's relevant groups approximately equal?	Yes	Yes[b]	Yes	Yes[b]
24. Was the funding for this study derived from a source that does not have a financial interest in its results?	No	Yes	No	Yes
25. Were the author's conclusions supported by the data in the results section?	Yes	Yes	Yes	Yes
Quality score	7.0	7.8	8.8	8.2
Quality rating	Moderate	Moderate	High	Moderate

[a] For this technology, blinding of patients is unlikely to influence change in disease management or clinical outcomes. Therefore, questions 13 and 14 receive an automatic "Yes" for this question even when studies did not blind patients.

[b] Although the followup times are not equal for the two groups, this is reflective of the nature of the technologies being compared. ELRs would never be used in clinical practice for a 1 year monitoring interval, while this is the normal monitoring interval for ILRs.

Table F-4. Results for Key Question 4 – Change in Disease Management

Publication	N	Length of follow-up (months)	Device	% patients receiving a diagnosis	Diagnoses	% patients with ECG-guided treatment changes	Types of treatment changes
Giada et al. 2007(53)	50	Mean: 321 ±235 days (ILR) 40 ±25 days (ELR)	Reveal Plus ILR ELR (without electrophysiological testing)	73 (19/26) 8.3% (2/24)	ILR: 6 SVT; 4 AF; 2 atrial flutter; 4 sinus tachycardia; 2 sinus bradycardia; 1 paroxysmal atrioventricular block ELR: 1 AF 1 SVT	73 (19/26) 8.3% (2/24)	4 ablation 8 antiarrhythmic therapy 4 anxiolytic therapy 3 pacemakers 1 ablation 1 antiarrhythmic therapy
Krahn et al. 2001(61)	60	12	ILR ELR (without tilt table + electrophysiological testing)	46.7 (14/30) 3.3 (1/30)	10 bradycardia, 3 vasovagal syncope, 1 narrow tachycardia 1 third degree AV block	46.7 (14/30) 3.3 (1/30)	10 pacemakers, 1 antiarrhythmic drugs, 3 dietary interventions 1 pacemaker
Rothman et al. 2007(11)	266	At least 25 days	MCOT remote continuous attended monitor ELR	87.3 (117/134) 74.2 (98/132)	NR	41.4 (55/134) 14.6 (19/132)	NR

NR – Not reported.

Table F-5. Results for Key Question 4 – Reduction in Syncope

Study	N	Resolution of syncope	
		ILR	ELR
Krahn et al. 2001(61)	60	13/14 primary diagnosed patients	6/6 diagnosed patients
		(numbers not reported for undiagnosed patients)	

Appendix G. Patient Care Infrastructure for Remote Cardiac Monitoring Devices

Table G-1. Patient Care Infrastructure for Remote Cardiac Monitoring Devices

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
Patient or event-activated external loop recorders (ELR)						
ER900 Series Cardiac Event Monitors(75,76)	Advanced Biosensor (Columbia, SC, USA) www.advancedbiosensor.com Braemar Inc. (Eagan, MN, USA) www.braemarinc.com	Transtelephonic or direct-to-PC	Manual download to PC	Optional	Software ECG analysis	NR
ER900L Cardiac Event Monitor(77)	Braemar Inc. (Eagan, MN, USA) www.braemarinc.com	Transtelephonic or direct-to-PC	Manual download to PC	Optional	Software ECG analysis	NR
Heart 2005A™ Transtelephonic ECG Loop Event Recorder(78)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com Cardiac Telecom (Greensburg, PA, USA) www.cardiactelecom.com	Transtelephonic transmission of ECG data to central monitoring lab.	Heartline Receiving Station (HRS)™ collects and stores data	Optional	Physician analysis of downloaded ECG	NR
Heart 2006™ Dual-Lead Transtelephonic ECG Loop Event Recorder(79)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com	Transtelephonic transmission of ECG data to central monitoring lab.	Heartline Receiving Station (HRS)™ collects and stores data	Optional	Physician analysis of downloaded ECG	NR

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
HeartView™ 12-Lead ECG Recorder/ Transmitter(80)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com	Transtelephonic or digital transmission of ECG data to central monitoring lab.	Heartline Receiving Station (HRS)™ collects and stores data	Optional	Physician analysis of downloaded ECG	NR
HeartView P12/8 PlusTM 12/8 ECG Personal Recorder/ Transmitter(81)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com	Transtelephonic or digital transmission of ECG data to central monitoring lab.	Heartline Receiving Station (HRS)™ collects and stores data	Optional	Physician analysis of downloaded ECG	NR
CG-6106 Personal 1-Lead ECG Monitor(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	Transtelephonic transmission of ECG data.	Receiving station collects and stores data	Optional	NR	NR
Genesis™(83)	Cardiac Evaluation Center (Milwaukee, WI) www.cec.net Lechnologies Research (Sussex, WI) www.lechnologies.com	Transtelephonic transmission of ECG data.	Central monitoring facility at CEC collects and stores data	Yes, 24 hours/day, 7 days/week. Staff training not reported.	Software ECG analysis	NR
Cardiophonics 1000 Memory Monitor(78,84)	Cardiophonics (Timonium, MD) www.cardiophonics.com	Transtelephonic transmission of ECG data.	Cardiophonics Arrhythmia Center collects and stores data.	Yes, by technicians (24 hours/day, 7 days/week)	NR	Technicians prepare a report for physician whenever event data are received.
E-Tac EX-1000 ECG Event Recorder(85)	Datrix (Escondido, CA) (no web address identified)	Transtelephonic transmission of stored ECG data	Compatible receiving station collects and stores data	Optional	NR	NR
TTM5000 Telephonic EKG Monitor(86)	HDS Medical (Laguna Niguel, CA) (Web site being remodeled)	Transtelephonic transmission of ECG data	NR	Optional	NR	NR

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
King of Hearts Express® Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	Transtelephonic transmission of ECG data	Download to PC	Optional	Software ECG analysis	NR
King of Hearts Express®+ Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	Transtelephonic transmission of ECG data	Download to PC	Optional	Software ECG analysis	NR
King of Hearts Express® AF Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	Transtelephonic or wireless (cell phone) transmission of ECG data.	Download to PC	Optional	Software ECG analysis	NR
MicroLR® Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	Transtelephonic transmission of ECG data.	Download to PC	Optional	Software ECG analysis	NR
LifeStar AF Express(88,89)	Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	Transtelephonic transmission of ECG data.	Life Watch monitoring center collects and stores data	Yes, by cardiac technicians (24 hours/day, 7 days/week)	Technicians analyze ECG data	Technicians prepare diagnostic reports in hard copy or online format, available to patient's physician. If predetermined criteria are met, the physician is notified immediately.
LifeStar AF Express(88,89)	Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	Transtelephonic transmission of ECG data.	Life Watch monitoring center collects and stores data	Yes, by cardiac technicians (24 hours/day, 7 days/week)	Technicians analyze ECG data	Technicians prepare diagnostic reports in hard copy or online format, available to patient's physician. If predetermined criteria are met, the physician is notified immediately.
LifeWatch Explorer(88,89)	Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	Transtelephonic transmission of ECG data.	Life Watch monitoring center collects and stores data	Yes, by cardiac technicians (24 hours/day, 7 days/week)	Technicians analyze ECG data	Technicians prepare diagnostic reports in hard copy or online format, available to patient's physician. If predetermined criteria are met, the physician is notified immediately.

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
PER (Personal ECG Recorder)(90,91)	Medical Monitors Ltd. (Eastgardens, Australia) www.medmon.com.au	Transtelephonic transmission of ECG data to a central monitoring station (Cardiocom).	Cardiocom automatic PC collects and stores data	Optional	Software ECG analysis	NR
CardioPAL SAVI™ Event Monitor(92)	Medicomp (Melbourne, FL, USA) www.medicompinc.com	Transtelephonic transmission of ECG data to a cardiac monitoring center. Attended 24/7.	Cardiac monitoring center collects and stores data	Yes, 24 hours, 7 days/week. Staff training not reported.	Software ECG analysis	NR
CardioPAL AI™ Event Monitor(92,93)	Medicomp (Melbourne, FL, USA) www.medicompinc.com	Transtelephonic transmission of ECG data to a cardiac monitoring center. Attended 24/7.	Cardiac monitoring center collects and stores data	Yes, 24 hours, 7 days/week. Staff training not reported.	Software ECG analysis	NR
CardioPAL™ Event Monitor(92)	Medicomp (Melbourne, FL, USA) www.medicompinc.com	Transtelephonic transmission of ECG data to a cardiac monitoring center. Attended 24/7.	Cardiac monitoring center collects and stores data	Yes, 24 hours, 7 days/week. Staff training not reported.	Software ECG analysis	NR
DR200E "Tel-a-heart"™ Event Recorder(94,95)	Northeast Monitoring (Maynard, MA) www.nemon.com	Transtelephonic or digital transmission of ECG data	Download to PC	Optional	Software ECG analysis	NR
R. Test Evolution 3 Event Monitor(96,97)	Novacor (Cedex, France) www.novacor.com	Transtelephonic transmission of ECG data. Software option allows transmission via modem or e-mail.	Either monitoring center or PC stores data	Optional	NR	NR

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
River-1 Electrocardiograph (ECG) Recorder and Transmitter(98)	SHL Telemedicine (Tel Aviv, Israel) www.shl-telemedicine.com	Transtelephonic or digital transmission of ECG data	NR	Optional	NR	NR
Heart Aide EZd(99,100)	TZ Medical (Portland, OR) www.tzmedical.com	Transtelephonic transmission of ECG data	NR	Optional	NR	NR
Hearttrak Smart AT and Hearttrak Smart^2(101)	Universal Medical (Ewing, NJ) (no web address identified)	Transtelephonic transmission of ECG data	NR	Optional	NR	NR
Vitaphone 3100 BT 1-Channel ECG Loop Recorder(102)	Vitasystems GmbH (Chemnitz, Germany) www.telemedsys.de/en	Wireless transmission of ECG data via Bluetooth™ technology.	Tele-ECG receiving system and workstation collects and stores data	Optional	Software ECG analysis	NR
Vitaphone 3300 BT 3-Channel ECG Loop Recorder(103)	Vitasystems GmbH (Chemnitz, Germany) www.telemedsys.de/en	Wireless transmission of ECG data via Bluetooth™ technology.	Tele-ECG receiving system and workstation collects and stores data	Optional	Software ECG analysis	NR
Cardiocall 20 and VS20 event recorders (can be used as loop recorder or post-event recorder)(104,105)	Delmar Reynolds Medical (Irvine, CA) www.delmarreynoldscom	Transtelephonic transmission or download of ECG data into a PC.	Delmar Reynolds Medical transtelephonic receiving center (Event Station) collects and stores data. Direct download also available.	Optional	NR	NR

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
eTrigger™ AF 920 (available in both looping and non-looping models)(106,155)	eCardio (Woodlands, TX) www.ecardio.com	Transtelephonic transmission of ECG data.	eCardio central lab collects and stores data in eCardioweb database	Yes, by certified monitoring technicians (24 hours, 7 days/week)	Certified monitoring technicians analyze downloaded ECG data	Technicians respond to event transmissions, report results according to physician directives and severity of event. Physician receives final report summary report at end of monitoring period
Patient or event-activated insertable loop recorders (ILR)						
REVEAL® PLUS Insertable Loop Recorder(32)	Medtronic (Minneapolis, MN, USA) www.medtronic.com	None during monitoring period. Patient visits physician's office for data retrieval.	Retrieval and analysis by Medtronic Programmer system	No	Software ECG analysis	NR
SLEUTH™ Implantable ECG Monitoring System(33)	Transoma Medical (Arden Hills, MN, USA) www.transomamedical.com	Wireless transmission of ECG data	Monitoring center collects and stores data	Yes	Data analysis at monitoring center	Final report sent to physician
Post-event recorders						
PER900 Post Event Recorder(107,108)	Advanced Biosensor (Columbia, SC, USA) www.advancedbiosensor.com Braemar Inc. (Eagan, MN, USA) www.braemarinc.com	Transtelephonic transmission of ECG data	Manual download to PC	Optional	Software ECG analysis	NR
HeartOne™(109)	Aerotel Medical Systems (Holon, Israel) www.aerotel.com	Transtelephonic transmission of ECG data to a central receiving station	Heartline Receiving Station (HRS)™ collects and stores data	Optional	Physician analysis of downloaded ECG	NR

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
CG-2206 Personal 1-Lead ECG Monitor(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	Transtelephonic transmission of ECG data	Receiving station collects and stores data	Optional	NR	NR
CG-5000 Minimonitor Transmitter(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	Transtelephonic transmission of ECG data	Receiving station collects and stores data	Optional	NR	NR
PMP4 SelfCheck™ ECG(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	During self-monitoring, The results are continuously transmitted to a PDA or cell phone during test performatnce via wireless Bluetooth technology. The data can then be transmitted wirelessly to the PMP Web Center and stored for review by physician or patient	PMP4 Web Center collects and stores data	Optional	Software ECG analysis	Web center notifies physician of new patient data.
CG-7100 Personal 12-Lead ECG Recorder(82)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com	Transtelephonic transmission of ECG data to a receiving station.	Receiving station collects and stores data	Optional	NR	NR
ecg@home(110)	H & C Medical Devices (Milan, Italy) (no web address identified)	Transtelephonic transmission or download of ECG data to PC	Manual download to PC	Optional	Physician analysis of downloaded ECG	NR

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
MEMORYTRACE™ Model 4224 Ambulatory ECG(111)	Hi-tronics Designs (Budd Lake, NJ) www.hitronics.com	Transtelephonic transmission of ECG data	Download to PC	Optional	Physician analysis of downloaded ECG	NR
MicroER® Recorder(87)	Instromedix (San Diego, CA, USA) www.instromedix.com	Transtelephonic transmission of ECG data	Download to PC	Optional	Software ECG analysis	NR
LifeWatch ER(88,89)	Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	Transtelephonic transmission of ECG data.	Life Watch monitoring center collects and stores data	Yes, by cardiac technicians (24 hours/day, 7 days/week)	Technicians analyze ECG data	Technicians prepare diagnostic reports in hard copy or online format, available to patient's physician. If predetermined criteria are met, the physician is notified immediately.
Micro™ ECG Recorder(112)	Medical Monitors Ltd. (Eastgardens, Australia) www.medmon.com.au	Transtelephonic transmission of ECG data to a central monitoring station (Cardiocom)	Cardiocom automatic PC collects and stores data	Optional	Software ECG analysis	NR
Cardiobeeper CB - 12/12(113,114,156)	SHL Telemedicine (Tel Aviv, Israel) www.shl-telemedicine.com	Transtelephonic transmission of ECG data	SHL monitor centers collect and store data. Alternatively, may be downloaded to PC if sent to doctor's office or hospital.	Yes, by trained nurses (24 hours, 7 days/week) if sent to SHL monitor centers	NR	If sent to SHLcenter, nurses advise patient on appropriate course of action or provide reassurance. If necessary, they dispatch an ambulance.

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
Cardiobeeper CB - 12L(115,116,156)	SHL Telemedicine (Tel Aviv, Israel) www.shl-telemedicine.com	Transtelephonic transmission of ECG data	SHL monitor centers collect and store data. Alternatively, may be downloaded to PC if sent to doctor's office or hospital.	Yes, by trained nurses (24 hours, 7 days/week) if sent to SHL monitor centers	NR	If sent to SHLcenter, nurses advise patient on appropriate course of action or provide reassurance. If necessary, they dispatch an ambulance.
Heart Aide(99,100)	TZ Medical (Portland, OR) www.tzmedical.com	Transtelephonic transmission of ECG data	NR	Optional	NR	NR
Vitaphone 100 IR ECG Post-Event Recorder(117)	Vitasystems GmbH (Chemnitz, Germany) www.telemedsys.de/en	Digital transmission of ECG data via infrared wireless link.	Tele-ECG receiving system and workstation collects and stores data	Optional	Software ECG analysis	NR
eTrigger™ AF 920 (available in both looping and non-looping models)(106,155)	eCardio (Woodlands, TX) www.ecardio.com	Transtelephonic transmission of ECG data	eCardio central lab collects and stores data in eCardioweb database	Yes, by certified monitoring technicians (24 hours, 7 days/week)	Certified monitoring technicians analyze downloaded ECG data	Technicians respond to event transmissions, report results according to physician directives and severity of event. Physician receives final summary report at end of monitoring period

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
Cardiocall event recorder (can be used as loop recorder or post-event recorder)(104,105)	Delmar Reynolds Medical (Irvine, CA) www.delmarreynoldscom	Transtelephonic transmission or download of ECG data into a PC	Delmar Reynolds Medical transtelephonic receiving center (Event Station) collects and stores data. Also can direct download into a PC.	Optional	NR	NR
Real-time continuous attended cardiac monitors						
CardioNet Mobile Cardiac Outpatient Telemetry (MCOT) System(18)	CardioNet, Inc. (San Diego, CA, USA) www.cardionet.com	Transtelephonic or cellular (wireless) transmission of ECG data to central monitoring station.	Data collected by CardioNet service center and stored.	Yes, by certified monitoring technicians (24 hours/day, 7 days/week)	Certified monitoring technicians analyze ECG data	Certified monitoring technicians "respond to events and report results as prescribed by referring physician". The physician receives a daily summary report by Internet, fax, or mail. Urgent events sent to physician immediately.
HEARTLink II arrhythmia detector and alarm system(1,118)	Cardiac Telecom (Greensburg, PA, USA) www.cardiactelecom.com	Processes radiofrequency-encoded transmitted ECG signals on the Tele-Link monitoring unit, which transmits them via telephone to a central monitoring lab.	Data collected by central monitoring lab and stored	Yes, by certified cardiac technicians 24 hours, 7 days/week. Event data generally reviewed within 12 seconds of receiving alarm.	Certified monitoring technicians analyze ECG data	Events viewed by "trained medical professionals and handled per protocol". Daily reports are sent to patient's physician

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
VST™ (Vital Signs Transmitter)(2,19)	Biowatch Medical (Grand Rapids, MI) www.biowatchmed.com	Transmission by cellular modem to central monitoring station	Data collected by Biowatch Medical's Clinical Monitoring Center, and stored. Patient's physician has continual access to data during monitoring period.	Yes, by nurses or critical care specialists	Certified critical care specialists or a licensed over-read physician interpret ECG data	If critical event occurs during monitoring, an accredited healthcare professional ensures that immediate intervention occurs. Patient's physician has access to patient reports at any time. At the end of the testing period, comprehensive patient summary reports are provided to the physician via the internet.
CG-6108 ACT (Ambulatory Cardiac Telemetry)(82) Also known as: LifeStar ACT™(89,119)	Card Guard Scientific Survival (Rehovot, Israel) www.cardguard.com Also marketed by: Life Watch (Buffalo Grove, IL) www.lifewatchinc.com	Transtelephonic or wireless (cell phone) transmission of ECG data. Automatically transmits to Life Watch monitroring center when an arrhythmia is detected.	Life Watch monitoring center collects and stores data	Yes, by cardiac technicians (24 hours/day, 7 days/week)	Technicians analyze ECG data	Technicians prepare diagnostic reports in hard copy or online format, available to patient's physician. If predetermined criteria are met, the physician is notified immediately.
Other devices - monitors with event-recording and Holter monitoring characteristics						
C.Net 2100 Monitor(120)	Cardionetics (Hampshire, UK) www.cardionetics.com	No transmission during monitoring period.	Download to printer in physician's office	No	Physician analyzes data	NR
DR200/HE Holter and Event Recorder(95,121)	Northeast Monitoring (Maynard, MA) www.nemon.com	Transtelephonic or digital transmission of ECG data	Download to PC	Optional	Software ECG analysis	NR

Device name	Manufacturer	Type of ECG transmission	Data collection	Attended monitoring?	Data analysis	Patient care
Pelex-04 Wireless ECG(122,123)	Pinmed (Pittsburgh, PA) www.pinmed.net	Transtelephonic, wireless, Wi-Fi, or Internet transmission of ECG data	NR	Optional	NR	NR