NICE National Institute for Health and Care Excellence

NICE guidance

Lead-I ECG devices for detecting symptomatic atrial fibrillation using single time point testing in primary care

Diagnostics guidance
Published: 8 May 2019

www.nice.org.uk/guidance/dg35

Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 There is not enough evidence to recommend the routine adoption of lead-I electrocardiogram (ECG) devices (imPulse, Kardia Mobile, MyDiagnostick and Zenicor-ECG) to detect atrial fibrillation when used for single time point testing in primary care for people with signs or symptoms of the condition and an irregular pulse. Further research is recommended to show how using lead-I ECG devices in this way affects:

- the number of people with atrial fibrillation detected, compared with current practice (see section 6.1) and
- primary and secondary care services, particularly how ECGs generated by the devices would be interpreted in practice, including staff time needed to interpret the ECG traces and associated costs (see section 6.2).

1.2 Centres currently using these devices for this indication are encouraged to take part in research and data collection (see sections 6.1 and 6.2).

2 Clinical need and practice

The problem addressed

2.1 Lead-I electrocardiogram (ECG) devices can be used in primary care to help detect atrial fibrillation in people presenting with signs or symptoms of the condition, who have an irregular pulse on manual pulse palpation. The devices include electrodes, internal storage for ECG recordings and automated software to interpret the ECG trace. Data can be transferred to a local or remote computer for further analysis by a healthcare professional.

2.2 Using lead-I ECG devices may improve detection of atrial fibrillation. This would lead to earlier identification of people who are at a higher risk of having a stroke and who would benefit from anticoagulant treatment. Using lead-I ECG devices would also allow ECGs to be quickly recorded when atrial fibrillation is suspected. This may help identify people with intermittent (paroxysmal) atrial fibrillation, which might have stopped before a 12-lead ECG can be done. The scope of this assessment is the use of the devices for single time point testing for people presenting in primary care with signs or symptoms of atrial fibrillation, and an irregular pulse.

The condition

Atrial fibrillation

2.3 Atrial fibrillation is a type of arrhythmia that causes an irregular or abnormally fast heart rate. It is the most common arrhythmia and has a higher incidence in older people. When a person has atrial fibrillation the upper chambers of the heart (the atria) beat irregularly, making the heart less effective at moving blood into the ventricles. This can cause blood clots to form, which may cause a stroke. Early detection of atrial fibrillation allows preventative treatment to be started, for example, oral anticoagulants to reduce the risk of stroke.

2.4 The abnormal electrical impulses that cause the condition can result in persistent, permanent or intermittent atrial fibrillation:

- permanent atrial fibrillation: atrial fibrillation is present all the time
- persistent atrial fibrillation: episodes last longer than 7 days (if left untreated)
- paroxysmal atrial fibrillation: intermittent episodes that usually last less than 2 days and stop without treatment.

2.5 Signs and symptoms of atrial fibrillation include feeling dizzy, being short of breath, feeling tired, having chest discomfort and heart palpitations. Atrial fibrillation can also be asymptomatic.

The diagnostics and care pathways

Diagnosis

2.6 NICE's guideline on atrial fibrillation recommends that manual pulse palpation should be used to assess for an irregular pulse, which may indicate underlying atrial fibrillation in people presenting with any of the following: breathlessness (dyspnoea), palpitations, syncope (dizziness), chest discomfort, stroke or transient ischaemic attack.

2.7 The guideline also recommends doing an ECG in all people, whether symptomatic or not, when atrial fibrillation is suspected because an irregular pulse has been detected. In current practice a 12-lead ECG can be done in primary or secondary care and is interpreted by a trained healthcare professional. This would be used to confirm atrial fibrillation that is suspected based on manual pulse palpation, before treatment is started. When atrial fibrillation has already been diagnosed, a 12-lead ECG is important to identify any additional abnormalities, such as left ventricular hypertrophy, which need to be considered when deciding on further treatment.

2.8 After an irregular pulse is detected, if there is a delay until a 12-lead ECG is done, paroxysmal atrial fibrillation may have stopped and therefore won't be detected by the ECG. Clinical experts advised that lead-I ECGs

would be used in the diagnostic pathway for people with signs and symptoms of atrial fibrillation after manual pulse palpation has revealed an irregular pulse.

Care pathway

2.9 NICE's guideline on atrial fibrillation makes recommendations for the care of people diagnosed with atrial fibrillation:

- **Assessment of risk and treatment to lower risk of stroke:** This includes assessing stroke and bleeding risk using the CHA_2DS_2VASc and HAS-BLED scores, and treatments to lower the risk of stroke (apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist). NICE has produced technology appraisal guidance on the direct oral anticoagulants apixaban, dabigatran etexilate and rivaroxaban and on edoxaban.
- **Treatment to control heart rate and rhythm**: This includes different interventions that are offered as part of a rate control strategy (beta blockers, calcium channel blocker, digoxin) or rhythm control strategy (pharmacological or electrical rhythm control or both), when appropriate.

  The guideline also covers the use of left atrial ablation if drug treatment has failed to control atrial fibrillation symptoms or is unsuitable.

3 The diagnostic tests

The assessment compared 5 interventions with 1 comparator.

The interventions

3.1 The lead-I electrocardiogram (ECG) devices were assessed when they were used in addition to 12-lead ECGs. Clinical experts advised that a 12-lead ECG would still be used after lead-I ECGs to identify any additional abnormalities, such as left ventricular hypertrophy, which need to be considered when deciding on further treatment. One of the 5 lead-I ECG devices in the scope, the RhythmPad GP (Cardiocity Ltd), was removed from this guidance after consultation. This was because the company informed NICE that, following a change in the CE mark, the device is no longer intended for detecting atrial fibrillation in people with signs or symptoms using single time point testing in primary care.

imPulse

3.2 imPulse (Plessey Semiconductors Ltd) is a CE-marked lead-I ECG device, which is provided with downloadable software for data analysis (imPulse Viewer). The software has to be installed on a personal computer or tablet. ECGs are taken by holding the device in both hands and placing each thumb on a separate sensor on the device for a pre-set length of time (from 30 seconds to 10 minutes). Data are transferred to the hardware hosting the analytical software using Bluetooth, with the recorded ECG trace being displayed in real time.

3.3 Once the recording has finished, the generated ECG trace can be saved in the imPulse viewer. Previously recorded ECG traces can also be loaded into this viewer and can be saved as PDFs. The software's atrial fibrillation algorithm analyses the trace and states whether atrial fibrillation is unlikely, possible or probable. For a 'possible' or 'probable' result, the company recommends that the person should have further investigations, and that the algorithm should not be used to definitively diagnose atrial fibrillation.

Kardia Mobile

3.4 Kardia Mobile (AliveCor Ltd) is a CE-marked lead-I ECG device that works with the Kardia app to record and interpret ECGs. A compatible Android or Apple smartphone or tablet is also needed. Two fingers from each hand are placed on the Kardia Mobile to record an ECG, which is sent wirelessly to the device hosting the Kardia app. The default length of recording is 30 seconds, but this can be extended up to 5 minutes. The ECG trace is then automatically sent as an anonymous file to a server in the European Union for storage as an encrypted file.

3.5 The app's algorithm classifies ECG traces as:

- normal
- possible atrial fibrillation detected
- unclassified.

The instructions for use state that the Kardia app assesses for atrial fibrillation only, and the device will not necessarily detect other cardiac arrhythmias. Any non-atrial fibrillation arrhythmias detected, including sinus tachycardia, are labelled as unclassified. The company states that any ECG labelled as 'possible atrial fibrillation' or 'unclassified' should be reviewed by a cardiologist or qualified clinician. ECG traces recorded by the device can be sent from a smartphone or tablet by email as a PDF attachment and stored in a patient's records.

MyDiagnostick

3.6 MyDiagnostick (MyDiagnostick Medical BV) is a CE-marked handheld lead-I ECG device that can produce and interpret an ECG trace. The ECG is generated by holding metal electrodes at each end of the device for 1 minute. The device activates automatically when gripped and deactivates automatically when released. A light on the device turns green if no atrial fibrillation is detected, or red if atrial fibrillation is detected. If an error occurs during the reading, the device produces both an audible warning and a visible warning from the light on the device. Up to 140 ECG traces can be stored in the device before it starts to

overwrite previous traces.

3.7 MyDiagnostick can be connected to a computer via a USB connection to download the generated ECG trace for review and storage using free software (downloaded from the MyDiagnostick website). The company states that the device automatically interprets ECGs, but that a clinical professional should examine the ECG trace to confirm the diagnosis.

Zenicor-ECG

3.8 Zenicor-ECG (Zenicor Medical Systems AB) is a CE-marked system with 2 components: a lead-I ECG device (Zenicor-EKG 2) and an online system for analysis and storage (Zenicor-EKG Backend System version 3.2). The online system sends data to a server in the European Union. This can be accessed using a web browser without prior installation of software and requires a user licence. ECGs are taken by placing both thumbs on the device for 30 seconds.

3.9 Once an ECG is taken using Zenicor-EKG 2, the trace can be transferred from the device (using a built-in mobile network modem) to a Zenicor server in Sweden. Here the ECG is analysed using the Zenicor-EKG Backend System, which includes an automated algorithm. This categorises an ECG into 1 of 12 groups of potential arrhythmias; 1 of which includes atrial fibrillation. The algorithm also reports if the ECG cannot be analysed. The company states that a clinician needs to manually interpret the ECG trace generated by the Zenicor-ECG to make a final diagnosis of atrial fibrillation. Clinicians can view the analysis using the Zenicor Doctor System user interface via a web browser. The ECG trace is also available via this interface and can be downloaded or printed as a PDF.

The comparator

12-lead ECG after an irregular pulse is detected

3.10 The comparator for this assessment is a 12-lead ECG, used to check for atrial fibrillation after an irregular pulse has been detected by manual

pulse palpation. Clinical experts commented that an irregular pulse on manual pulse palpation is not thought to be sufficient to start anticoagulant treatment, so in this diagnostic pathway patients do not have treatment until a 12-lead ECG confirms atrial fibrillation.

3.11 Clinical experts commented that there can be delays in arranging 12-lead ECGs after an irregular pulse is detected, which can delay diagnosis of atrial fibrillation, or potentially miss paroxysmal atrial fibrillation because the initial examination did not include an ECG recording. The length of this delay will vary and depends on local arrangements for doing 12-lead ECGs, for example, if this can be done in primary care or if a referral to secondary care is needed.

4 Evidence

The diagnostics advisory committee (section 8) considered evidence on lead-I electrocardiogram (ECG) devices (imPulse, Kardia Mobile, MyDiagnostick and Zenicor-ECG) for detecting atrial fibrillation using single time point testing in primary care from several sources. Full details of all the evidence are in the committee papers. Evidence on the RhythmPad GP was removed from this guidance after consultation (see section 3.1). To make sure the committee papers are clear, the published diagnostics assessment report and extra relevant documents include the evidence assessed on RhythmPad GP.

Clinical effectiveness

4.1 The external assessment group (EAG) did a systematic review to identify evidence on the diagnostic accuracy and clinical effectiveness of using the lead-I ECG devices to detect atrial fibrillation. Included studies were those that used the devices at a single time point to detect atrial fibrillation (rather than repeated use over a period of time). Because no studies were identified in the population of interest (people with signs and symptoms of atrial fibrillation and an irregular pulse on manual palpation), the EAG included studies done in a population who were asymptomatic. The EAG included in this definition people who did not present with signs and symptoms of atrial fibrillation (for example, breathlessness or palpitations) with or without a previous diagnosis of atrial fibrillation. It included people with other cardiovascular comorbidities and people who were attending a cardiovascular clinic.

4.2 The EAG divided their review into 2 parts; studies reporting diagnostic accuracy of the devices and studies reporting the clinical effectiveness of the devices.

Diagnostic accuracy

4.3 In the diagnostic test accuracy review, 9 studies were included. There is an overview of the included studies in table 1. All the studies either enrolled people with a known atrial fibrillation status (that is, people known to have atrial fibrillation and people with no history of the

condition), or who were recruited from cardiology services. Only Desteghe et al. (2017) provided the reasons people were admitted to a cardiology service, with 3.4% admitted because of symptomatic atrial fibrillation.

4.4 Only 1 study was done in primary care (Vaes et al. 2014), with the rest in secondary or tertiary care. There was 1 study done in the UK (Williams et al. 2015). No published studies assessed the imPulse device.

4.5 In all studies the reference standard was a 12-lead ECG interpreted by a trained healthcare professional (a cardiologist, electrophysiologist or GP with a special interest in cardiology). The index test (lead-I ECG) and reference standard (12-lead ECG) were both done within 6 hours of each other in all but 1 study (Vaes et al.). In this study the interval between tests was not reported.

Table 1 Overview of studies included in the EAG's diagnostic accuracy review

Device	Study	Population in study	Interpreter of device output
Kardia Mobile	Desteghe et al. 2017[a] (Belgium)	Inpatients in a cardiology ward (35.6% had a history of atrial fibrillation)	• Electrophysiologists • Algorithm Results presented separately
	Haberman et al. 2015 (USA)	Cardiology clinic patients[b]	Electrophysiologist
	Koltowski et al. 2017[c] (Poland)	People in tertiary care	Cardiologist

	Lau et al. 2013 (Australia)	People at a cardiology department (24% had a history of atrial fibrillation)	Algorithm
	Williams et al. 2015 (UK)	People attending an atrial fibrillation clinic who were known to have atrial fibrillation and people with unknown atrial fibrillation status (who were attending the clinic for reasons unrelated to atrial fibrillation)	• Cardiologist • GP with special interest in cardiology Results presented separately
MyDiagnostick	Desteghe et al. 2017[a] (Belgium)	Inpatients in a cardiology ward (35.6% had a history of atrial fibrillation)	• Electrophysiologists • Algorithm Results presented separately
	Tieleman et al. 2014 (Netherlands)	People attending an outpatient cardiology clinic or a specialised atrial fibrillation outpatient clinic	Algorithm
	Vaes et al. 2014 (Belgium)	People known to have atrial fibrillation (83.4%) and people with no history of the condition invited to take part by GPs	Algorithm
Zenicor-ECG	Doliwa et al. 2009 (Sweden)	People with atrial fibrillation, atrial flutter or sinus rhythm attending a cardiology outpatient clinic	Cardiologist

[a] Desteghe et al. assessed both Kardia Mobile and MyDiagnostick.

[b] Results from additional study participants (healthy young adults and elite athletes) were not included in the EAG's analyses.

[c] Koltowski et al. was only available as a conference proceeding.

Quality assessment of diagnostic accuracy studies

4.6 The QUADAS-2 tool was used to assess study quality. For patient selection, the EAG judged that all 9 studies had an unclear risk of bias and a high level of concern for applicability (because none were done in a population who had symptoms). For 1 study there was limited information available in the publication; Koltowski et al. (2017) was only available as a conference proceeding.

4.7 The included studies varied in how the devices gave a positive result for atrial fibrillation. This was either based on the lead-I ECG device's diagnostic algorithm or on clinician interpretation of an ECG trace generated by the devices. The EAG judged that studies in which the device output was interpreted by a trained healthcare professional were more applicable (low concern) than those in which a lead-I ECG device algorithm alone was used (high concern; Lau et al. 2013, Tieleman et al. 2014 and Vaes et al. 2014). The EAG presented results in 2 sections depending on how atrial fibrillation was identified (by a clinician or by the device's algorithm alone).

Diagnostic accuracy results: Lead-I ECG interpreted by a trained healthcare professional

4.8 Data were included from 4 studies, which assessed Kardia Mobile alone (Haberman et al. 2014; Williams et al. 2015), Kardia Mobile and MyDiagnostick (Desteghe et al. 2017) and Zenicor-ECG alone (Doliwa et al. 2009).

4.9 Desteghe et al. reported separate accuracy estimates from lead-I ECGs interpreted by 2 electrophysiologists; only pooled estimates using data from electrophysiologist 1 are shown in table 2 (values were similar when data from electrophysiologist 2 were used). Williams et al. reported separate accuracy estimates from lead-I ECGs interpreted by a cardiologist or by a GP with a special interest in cardiology. Pooled accuracy estimates in table 3 used data from Williams et al. when the lead-I ECG interpreter was a cardiologist (interpreters in other studies were cardiologists or electrophysiologists). Pooled accuracy estimates using data from Williams et al. when the interpreter was a GP with a

special interest in cardiology (not shown) were similar. However, the study showed a decrease in specificity when the GP interpreted the lead-I ECG; 76% (95% confidence interval [CI] 64% to 85%) compared with 86% (95% CI 76% to 94%) when the cardiologist interpreted them.

Table 2 Pooled diagnostic accuracy estimates for lead-I ECGs interpreted by a trained healthcare professional

Meta-analysis	Lead-I devices in included studies (number of studies)	Pooled sensitivity % (95% CI)	Pooled specificity % (95% CI)
All devices[a,c]	Kardia Mobile (3[b,d]), Zenicor-ECG (1[e])	93.9 (86.2 to 97.4)	96.5 (90.4 to 98.8)
All devices[a,c]	Kardia Mobile (2), MyDiagnostick (1[b,f]), Zenicor-ECG (1[e])	90.8 (83.8 to 95.0)	95.6 (89.4 to 98.3)
Kardia Mobile[a,c]	Kardia Mobile (3[d])	94.0 (85.1 to 97.7)	96.8 (88.0 to 99.2)

[a] Data from electrophysiologist 1 from Desteghe et al. 2017.

[b] Data from Desteghe et al. 2017 from either Kardia Mobile or MyDiagnostick.

[c] Data from Williams et al. 2015 from cardiologist interpreting lead-I ECG.

[d] Desteghe et al. 2017; Haberman et al. 2015; Williams et al. 2015.

[e] Doliwa et al. 2009.

[f] Desteghe et al. 2017.

4.10 Only Kardia Mobile had sufficient studies to produce a device-specific pooled estimate (see table 2). Accuracy estimates from individual studies for other devices are presented in table 3. The EAG commented that there were insufficient data to formally assess differences between the lead-I ECG devices.

Table 3 Individual study diagnostic accuracy estimates for lead-I ECGs interpreted by a trained healthcare professional

Lead-I ECG device	Study	Sensitivity % (95% CI)	Specificity % (95% CI)
MyDiagnostick[a]	Desteghe et al. 2017	85.0 (62.0 to 97.0)	95.0 (92.0 to 98.0)
Zenicor-ECG	Doliwa et al. 2009	92.0 (81.0 to 98.0)	96.0 (86.0 to 100.0)
[a] Data from electrophysiologist 1 from Desteghe et al.			

Diagnostic accuracy results: ECG trace interpreted by the device's algorithm

4.11 Four studies that reported sensitivity and specificity of the lead-I ECG device when the trace was interpreted by the device's algorithm alone were included in meta-analyses. Two studies reported data for MyDiagnostick alone (Tieleman et al. 2014; Vaes et al. 2014), 1 study for Kardia Mobile alone (Lau et al. 2013) and 1 study for both MyDiagnostick and Kardia Mobile (Desteghe et al. 2017). Pooled sensitivity and specificity estimates from meta-analyses are presented in table 4.

Table 4 Pooled diagnostic accuracy estimates for lead-I ECG traces interpreted by device algorithm alone

Meta-analysis	Lead-I devices in included studies (number of studies)	Pooled sensitivity % (95% CI)	Pooled specificity % (95% CI)
All devices[a]	Kardia Mobile (1[b]), MyDiagnostick (3[c])	96.2 (86.0 to 99.0)	95.2 (92.9 to 96.8)
All devices[a]	Kardia Mobile (2[d]), MyDiagnostick (2[e])	95.3 (70.4 to 99.4)	96.2 (94.2 to 97.6)
MyDiagnostick	MyDiagnostick (3[c])	95.2 (79.0 to 99.1)	94.4 (91.9 to 96.2)

Kardia Mobile	Kardia Mobile (2[d])	88.0 (32.3 to 99.1)	97.2 (95.1 to 98.5)

[a] Data from Desteghe et al. 2017 from either Kardia Mobile or MyDiagnostick.

[b] Lau et al. 2013.

[c] Desteghe et al. 2017; Tieleman et al. 2014; Vaes et al. 2014.

[d] Desteghe et al. 2017; Lau et al. 2013.

[e] Tieleman et al. 2014; Vaes et al. 2014.

4.12 The EAG noted that the companies who make the lead-I ECG devices stated that atrial fibrillation should not be diagnosed using the algorithm alone; ECG traces produced by the devices should be reviewed by a qualified healthcare professional.

Comparisons between lead-I ECG devices

4.13 The EAG commented that the available data were not sufficient to formally assess differences between the different lead-I ECG devices. Desteghe et al. (2017) assessed the concordance between Kardia Mobile and MyDiagnostick. There was no statistically significant difference in agreement between the devices (based on kappa values) when assessing all patients (p=0.677) or after excluding those with an implanted device (for example, a pacemaker or implantable cardiac defibrillator; p=0.411).

4.14 The EAG commented that the pooled sensitivity and specificity values were similar across all the meta-analyses done, irrespective of how the lead-I ECG trace was interpreted (algorithm or healthcare professional) or which lead-I ECG devices were used (pooled estimates produced by the EAG used Kardia Mobile, MyDiagnostick and Zenicor-ECG).

Diagnostic accuracy results: further studies excluded from the EAG's main report

4.15 The EAG identified further studies that reported sensitivity and specificity estimates of the lead-I ECG devices. However, it did not include them in its main report because they did not meet 1 of the

eligibility criteria for inclusion, that is, that the reference standard in the studies was not a 12-lead ECG interpreted by a trained healthcare professional. Results were presented in appendix 6 of the diagnostics assessment report. They included 1 unpublished study which assessed imPulse (no other studies were identified for this device). Ranges were reported for sensitivity (67% to 100%) and specificity (83% to 100%). These data were used in the economic model.

Evidence on clinical effectiveness of the lead-I ECG devices

4.16 The EAG included 19 studies in its clinical effectiveness review. Of these, 7 studies were done in primary care (Orchard et al. 2014; Chan et al. 2016; Chan et al. 2017; Gibson et al. 2017; Hussain and Thakrar, 2016; Kaasenbrood et al. 2016; Orchard et al. 2016). There were 2 studies done in the UK (Gibson et al. 2017; Hussain and Thakrar, 2016). Of the studies, 13 included data for Kardia Mobile, 5 for MyDiagnostick, 1 for Zenicor-ECG and 1 for imPulse. No studies were identified that assessed the clinical effectiveness of lead-I ECG devices when used for people with signs and symptoms of atrial fibrillation presenting in primary care.

Diagnostic yield

4.17 There were 13 studies that reported diagnostic yield of atrial fibrillation detection by lead-I ECG devices (various devices), which ranged from 0.38% to 5.84%. However, the location of testing varied between studies; primary care (6 studies), secondary care (2 studies), tertiary care (1 study) and in the community (4 studies). In the primary care studies, the range was 0.49% to 5.84%. None of the studies assessed people with signs and symptoms of atrial fibrillation. The enrolled populations varied from the general population or people who were attending primary care for a reason unrelated to atrial fibrillation (for example, for flu vaccination) to people admitted to a cardiology ward and people with known atrial fibrillation. The prevalence of atrial fibrillation in these populations is likely to vary and may not be applicable to the population that is the focus of this assessment. No data were found on any benefit of lead-I ECGs in identifying people with paroxysmal atrial fibrillation, compared with later ECG testing.

Test failure rate

4.18 Test failure rate (which included both the device failing to produce a result and producing a poor-quality ECG trace) varied between 0.1% and 9% (various devices). Reasons suggested for uninterpretable lead-I ECGs were sinus tachycardia or bradycardia, that patients had a tremor or that hospitalised patients were unable to hold the devices firmly enough.

Time to diagnosis of atrial fibrillation

4.19 A study done in Australia (Lowres et al. 2014) reported a time to diagnosis of atrial fibrillation of 16.6 days (standard deviation of 14.3 days) from detection by an initial lead-I ECG diagnostic test at a pharmacy to confirmed diagnosis with a 12-lead ECG.

Ease of use of devices

4.20 Tieleman et al. (2014) reported that people were able to use MyDiagnostick with minimal instructions. Chan et al. (2017) reported that Kardia Mobile was easy to use. Orchard et al. (2016) commented that it may be difficult for older people to hold the Kardia Mobile device still enough to take a reading. In Desteghe et al. (2017), 7% of people were excluded from the study because they could not hold the devices as intended (the study used both MyDiagnostick and Kardia Mobile).

Effect on clinical decision making

4.21 In Hussain and Thakrar (2016), 5 out of 6 people had a change in the clinical management of their condition after atrial fibrillation was detected by Kardia Mobile (1 person died as an inpatient after referral to hospital). In Lowres et al. (2014), oral anticoagulants were prescribed for 6 out of 10 new patients with atrial fibrillation detected by a lead-I ECG followed by a 12-lead ECG interpreted by a cardiologist.

Evidence on patient- and healthcare professional-reported outcomes

4.22 In Orchard et al. (2016), which used Kardia Mobile, patients and GPs commented that they liked using the device. Chan et al. (2017) reported

that all patients asked were willing to have further testing with Kardia Mobile at future GP visits, and 86% of GPs surveyed considered that the device was useful for atrial fibrillation screening and they would use it in their daily practice. Gibson et al. (2017) reported generally positive responses to using MyDiagnostick, although some issues with implementing use of the device were raised. A further study reported that Kardia Mobile was easily administered and that no one declined testing with the device (Hussain and Thakrar 2016). In Chan et al. (2017), interviewed patients commented that having access to the lead-I ECG device in the surgery was more convenient than having to attend another healthcare facility for a 12-lead ECG.

'Real world' data

4.23 The EAG also looked at unpublished evidence from a quality control audit on the use of Kardia Mobile across Eastbourne, Hailsham and Seaford clinical commissioning group and Hastings and Rother clinical commissioning group. This was provided by a specialist committee member as an example of an ongoing audit. Over a 2-year period the device was used in primary care or for home visits if people had an irregular pulse or signs of atrial fibrillation. There were 183 ECG traces reported, identifying 128 cases of atrial fibrillation from the lead-I ECG trace alone. The proportion of people newly diagnosed with atrial fibrillation (69.9%) was considerably higher than the diagnostic yield in studies identified by the EAG (0.38% to 5.84%), although the audit was designed for quality control, and not to assess atrial fibrillation yield.

Cost effectiveness

Systematic review of cost-effectiveness evidence

4.24 The EAG did a systematic review to identify published full economic evaluations of lead-I ECG devices for detecting atrial fibrillation. Studies were excluded if they assessed the devices for repeated ECG measurements (rather than at a single time point) or if they assessed the devices for screening a population or for an asymptomatic 'silent atrial fibrillation' population. The EAG did not identify any published studies

that met their inclusion criteria. However, the EAG highlighted 2 recently published economic evaluations (Welton et al. 2017 and Jacobs et al. 2018) that suggested that lead-I ECG devices may represent a cost-effective use of resources for systematic, opportunistic screening of people aged 65 years and over during a routine GP appointment.

Modelling approach

4.25 The EAG developed a de novo economic model designed to evaluate the cost effectiveness of using the lead-I ECG devices for single time point testing of people presenting in primary care with signs and symptoms of atrial fibrillation and who have an irregular pulse.

Model structure

4.26 The model compared the effect of using a lead-I ECG device in primary care for people with signs and symptoms of atrial fibrillation who have an irregular pulse (detected by manual pulse palpation) with standard diagnostic testing (that is, without the use of a lead-I ECG device). The model was in 2 phases: a diagnostic phase followed by a post-diagnostic phase.

Diagnostic phase

4.27 This phase covered the initial assessment of people presenting in primary care with signs and symptoms of atrial fibrillation, and who have had manual pulse palpation that shows an irregular pulse. The model compared 2 strategies: referral for a subsequent 12-lead ECG to check for atrial fibrillation (standard diagnostic pathway) or having a lead-I ECG in primary care at the same primary care appointment to check for atrial fibrillation (lead-I ECG pathway) followed by a 12-lead ECG if the clinician thought this was appropriate.

4.28 The diagnostic phase model covered the first 3 months after the initial primary care appointment. By the end of the diagnostic phase, people have either been diagnosed as having atrial fibrillation, or no atrial fibrillation has been detected (either correctly or incorrectly). People diagnosed with atrial fibrillation can have anticoagulants and rate control

treatment (beta blockers).

4.29 People can have up to 2 cerebrovascular events (transient ischaemic attack, ischaemic or haemorrhagic stroke), a non-major bleeding event, or die. This was modelled using a Markov model. The probability of having a cerebrovascular event for people with atrial fibrillation is reduced if they are taking anticoagulants. However, anyone taking anticoagulants has an associated higher risk of having a bleeding event.

Post-diagnostic phase

4.30 After the 3-month diagnostic phase model, people entered a second Markov model. This had the same structure as the Markov model in the diagnostic phase after a diagnosis has been made, but ran over a 30-year timespan (with 3-month cycles). People entered based on their history of cerebrovascular events (none, 1 or 2) and they could have further cerebrovascular events, non-major bleeding events, or die.

Model inputs

4.31 The starting age of the modelled cohort was 70 years, and the model was run over 30 years. The cohort consisted of people with signs and symptoms of atrial fibrillation including an irregular pulse. This included people with atrial fibrillation (assumed to be 20% based on clinical advice) and people without the condition (assumed to have either atrial or ventricular ectopy).

Diagnostic accuracy of lead-I ECG devices

4.32 Estimates of the diagnostic accuracy of the 4 lead-I ECG devices were obtained from the EAG's systematic review and meta-analyses. The EAG used estimates of accuracy based on healthcare professionals interpreting the ECG traces, because it assumed that atrial fibrillation would not be diagnosed based on a device's algorithm alone.

Table 5 Sensitivity and specificity values of lead-I ECG devices used in the economic model

Lead-I ECG	Interpreter of ECG	Data source	Sensitivity %	Specificity %
imPulse	Healthcare professional	Reeves (unpublished)	83.5[a]	91.5[a]
Kardia Mobile[b]	Healthcare professional	Pooled analysis[c]	94.0	96.8
MyDiagnostick	Healthcare professional	Desteghe et al. (2017)[d]	85.0	95.0
Zenicor-ECG	Healthcare professional	Doliwa et al. (2009)	92.0	96.0

[a] EAG used the midpoint from the range reported in the Reeves report.

[b] Alternative accuracy estimates based on a pooled estimate in which data from electrophysiologist 2 from Desteghe et al. were used in a scenario analysis; sensitivity 91.3%, specificity 97.4%.

[c] Pooled estimate from 3 studies; see table 2.

[d] Desteghe et al. reported accuracy estimates from 2 electrophysiologists. Estimates used in the base case were from electrophysiologist 1 (see table 3); values from electrophysiologist 2 were used in a scenario analysis (sensitivity of 80.0%, specificity of 98.0%).

Treatment effects: mortality and cerebrovascular events

4.33 For people with atrial fibrillation, the rate of mortality and cerebrovascular events (transient ischaemic attack, ischaemic or haemorrhagic stroke) in people who did not have anticoagulants was taken from Sterne et al. (2017). The effect of anticoagulants on the incidence of these events in people with atrial fibrillation was also taken from this study. For people without atrial fibrillation the rate of mortality and cerebrovascular events was taken from various sources (for example, Public Health England report, Office for National Statistics report, Rothwell et al. 2005). The risk of cerebrovascular events and mortality for people with untreated atrial fibrillation does not vary by type

of atrial fibrillation. That is, risk is the same for paroxysmal, permanent and persistent atrial fibrillation. After people have a cerebrovascular event, their risk of mortality increases. The EAG assumed that this risk was 2.6 times greater based on a study of stroke survivors in Norway (Mathisen et al. 2016). The risk of having a further cerebrovascular event was based on a meta-analysis of stroke survivors (Mohan et al. 2011) with increased risk in the first year, then a lower risk from year 2 onwards.

Treatment effect: clinically relevant bleeding

4.34 The risk of clinically relevant bleeding is increased for people who have anticoagulants, based on Sterne et al. (2017). This is the case for people with or without atrial fibrillation.

Costs

Lead-I ECG device costs

4.35 Annual costs of the devices used in the base-case model are shown in table 6. Because the lead-I ECG could be used outside the scope of this assessment, the EAG also did a scenario analysis that excluded the costs of the devices. No extra cost was included for administering and interpreting the lead-I ECG because it was assumed that this could be done during a standard GP consultation.

Table 6 Estimated annual costs of lead-I ECG devices

Lead-I ECG	Item	Unit cost (£)[c]	Expected lifespan (years)	Annual cost (£)	Unit cost per test[b] (£)
imPulse	Device	175	2	87.50	1.62
Kardia Mobile	Device	82.50	5	16.50[a]	0.31
MyDiagnostick	Device	450	5	90	1.67

Zenicor-ECG	Device and 36-month licence	1,980	10	613.27	11.40
	Extra 36-month licence	1,780	3		

[a] Costs of any additional tablet or device needed not included (the effect of this additional cost is assessed in scenario analysis F).

[b] Assumes 54 people tested per year.

[c] Excluding VAT.

Costs of 12-lead ECGs and Holter monitoring

4.36 The EAG devised base cases that differed depending on where 12-lead ECGs were done. If a 12-lead ECG was done in primary care, the cost of administering it was assumed to be £12.34. This was based on the costs of the device, disposables and staff time to do and interpret the ECG. The cost of administering a 12-lead ECG in secondary care was assumed to be £52 (from NHS reference costs). The cost of Holter monitoring (for 7 days) was assumed to be £120.23.

Treatment and event costs

4.37 Costs for anticoagulant (apixaban) and rate control (beta blockers) treatment were obtained from the British national formulary and NHS drug tariff. Costs of bleeding events and transient ischaemic attack were taken from NHS reference costs. Age and sex-adjusted 1- and 5-year costs for strokes were from the Sentinel Stroke National Audit Programme's cost and cost-effectiveness report (2016).

Health-related quality of life and QALY decrements

4.38 Berg et al. (2010) was used to provide utility values for people with atrial fibrillation (see table 7). Beta blockers were assumed to improve symptoms for people with atrial fibrillation.

Table 7 Utility values used in base-case economic model (at age 70; age- and sex-adjusted)

	Atrial fibrillation status (95% CI)	
	Atrial fibrillation	**No atrial fibrillation**
Untreated	0.665 (0.537 to 0.881)	0.744 (0.480 to 0.942)
Treated	0.744 (0.480 to 0.942)	0.744 (0.480 to 0.942)

4.39 People without atrial fibrillation were assumed to be having a short symptomatic episode caused by atrial or ventricular ectopy that resolved quickly. For people who had an ischaemic or haemorrhagic stroke, a lifetime utility decrement was applied at the time of the first stroke (no further decrements were applied for subsequent strokes). The size of the decrement was −0.272 (95% CI −0.345 to −0.198) for both types of stroke. Transient ischaemic attacks and bleeding events were assumed to have no long-term effect on health-related quality of life, and no utility decrement was applied for these events.

Base-case assumptions

4.40 The following assumptions were applied in the base-case analyses:

- Of the people presenting in primary care with signs and symptoms of atrial fibrillation, and who have an irregular pulse, 20% have atrial fibrillation.
- Of the people with atrial fibrillation, 50% have paroxysmal atrial fibrillation. The EAG commented that there is a lack of evidence on the prevalence of paroxysmal atrial fibrillation in people with symptoms, and noted that a recent study (Welton et al. 2017) had reported wide variation in prevalence (although not necessarily in a symptomatic population). The effect of varying this prevalence was investigated in sensitivity analysis.
- Additional interpretation by a cardiologist is needed for 10% of lead-I ECG tests.
- The 12-lead ECGs have 100% sensitivity and specificity for atrial fibrillation (if a person is in atrial fibrillation at the time of the test).

- For 48% of people with paroxysmal atrial fibrillation the episode will have stopped by the time a 12-lead ECG is done (2 or 14 days after the initial primary care consultation when an irregular pulse is detected). This is based on data from Israel et al. (2004).
- Holter testing for paroxysmal atrial fibrillation is assumed to have 100% sensitivity and specificity (if atrial fibrillation occurs during testing). Holter testing is assumed to be for 7 days and 70% people with atrial fibrillation are assumed to have an episode in that time (based on data from Kirchoff et al. 2006).
- In the standard diagnostic pathway, 50% of people who have a negative 12-lead ECG have Holter testing. In the lead-I ECG pathway, 80% of people who have a negative lead-I ECG have a 12-lead ECG. If the 12-lead ECG is negative, 50% of people have Holter testing. Of the 20% of people who are not referred for a 12-lead ECG after a negative lead-I ECG, 50% have Holter testing.
- Only people who are diagnosed with atrial fibrillation and who have a CHA_2DS_2-VASc score of 2 or more have anticoagulants. There are 82.4% of people with atrial fibrillation assumed to have a CHA_2DS_2-VASc score of 2 or more, and 81.2% of these are assumed to take anticoagulants (based on NHS Quality and Outcomes Framework 2016/2017 indicator AF007).
- People having anticoagulants have apixaban (simplifying assumption).
- Treatment with anticoagulants starts immediately after a positive lead-I ECG result (simplifying assumption).
- People whose atrial fibrillation is undetected and who have a cerebrovascular event are assumed to have their atrial fibrillation diagnosed as part of treatment.

Base-case results

4.41 The EAG produced 4 base cases, depending on when and where 12-lead ECGs were done:

- base case 1: 12-lead ECG in primary care (2 days later)

- base case 2: 12-lead ECG in primary care (14 days later)
- base case 3: 12-lead ECG in secondary care (2 days later)
- base case 4: 12-lead ECG in secondary care (14 days later).

4.42 In pairwise analyses, all the lead-I ECG devices were compared independently with the standard pathway (that is, no use of a lead-I ECG device). Results were similar across the 4 base cases, and in probabilistic analyses. The results from base-case 1 are shown in table 8.

Table 8 Base case 1: Pairwise cost-effectiveness analysis (compared with standard pathway)

	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£)
Standard pathway	514,187	447.963	–	–	–
Kardia Mobile	515,551	449.249	1,364	1.286	1,060
imPulse	530,745	448.987	16,557	1.024	16,165
MyDiagnostick	521,233	449.024	7,046	1.061	6,638
Zenicor-ECG	518,468	449.199	4,281	1.236	3,462

4.43 In fully incremental analyses across all the base cases, all lead-I ECG devices were dominated by Kardia Mobile (that is, Kardia Mobile cost less but produced more quality-adjusted life years [QALYs]). The incremental cost-effectiveness ratios (ICERs) for Kardia Mobile compared with the standard pathway were the same as for the pairwise comparison (less than £1,100 per QALY gained). At consultation, the company who makes MyDiagnostick proposed new costs for their device. The EAG ran the base-case analysis again using these costs in an addendum to the diagnostics assessment report. This resulted in lower costs for MyDiagnostick, but did not affect the EAG's overall conclusions on the pairwise cost-effectiveness analysis.

Analysis of alternative scenarios

4.44 The EAG investigated the effect of varying some of the base-case assumptions in scenario analyses. This included assessing the effect of adding the cost of a smartphone or tablet (including the cost of a data network) for Kardia Mobile in a threshold analysis. The EAG commented that a smartphone or tablet would need to cost more than £2,850 for Kardia Mobile to no longer dominate the other lead-I ECG devices. The ICER for Kardia Mobile compared with the standard pathway remained less than £20,000 per QALY gained if a smartphone or tablet costs less than £24,362. Using alternative accuracy estimates for MyDiagnostick and Kardia Mobile (using results from electrophysiologist 2 from Desteghe et al.) resulted in Kardia Mobile having an ICER of £5,503 per QALY gained compared with MyDiagnostick. Compared with the standard pathway MyDiagnostick dominated. The Zenicor-ECG was no longer dominated, but had an ICER of £242,994 per QALY gained when compared with Kardia Mobile.

Deterministic sensitivity analysis

4.45 The model was most sensitive to the proportion of patients whose atrial fibrillation was paroxysmal (assumed to be 50% in the base case) in one-way analyses for all of the lead-I ECG devices. Cost effectiveness improved as the proportion of paroxysmal atrial fibrillation increased. Conversely, lower estimates of the proportion of paroxysmal atrial fibrillation made the devices less cost effective (increased incremental costs and decreased incremental QALYs).

Probabilistic sensitivity analysis

4.46 In a probabilistic sensitivity analysis (done in base case 1) all other lead-I ECG devices were dominated by Kardia Mobile in a fully incremental analysis. In pairwise comparisons with the standard pathway, ICERs were similar to the deterministic results, and all were less than £17,000 per QALY gained.

5 Committee discussion

5.1 The committee discussed the effects of atrial fibrillation. The clinical experts commented that earlier diagnosis of atrial fibrillation may reduce a person's risk of stroke because anticoagulation treatment could be started sooner, if appropriate. Also, earlier treatment with rate control drugs, such as beta blockers, can stop associated symptoms and may improve quality of life, although both types of treatment are associated with a risk of side effects. Comments submitted by a patient expert highlighted that atrial fibrillation can go undiagnosed for months or even years. It is common for people to have anxiety, depression and fear while living with the symptoms of atrial fibrillation, particularly when the cause of the symptoms is unknown. If atrial fibrillation is not treated, people are at higher risk of a stroke. The clinical experts commented that atrial fibrillation-related stroke can be extremely disabling and debilitating, with family members often becoming full-time carers to the people affected. The committee was aware that improving detection of atrial fibrillation is therefore a priority for the healthcare system. It concluded that earlier diagnosis could be important to reduce the risk of stroke and its associated effects for people with the condition.

5.2 The committee asked how suspected atrial fibrillation is currently investigated in people presenting in primary care. The clinical experts commented that an electrocardiogram (ECG) is needed to determine whether atrial fibrillation is present, but delays in doing an ECG often prevent atrial fibrillation being diagnosed, particularly if it is paroxysmal. They explained that episodes of paroxysmal atrial fibrillation usually stop within 48 hours without treatment. This can lead to it being missed if an ECG is not done immediately. Earlier access to an ECG, such as a lead-I ECG that can be done during a GP consultation, would increase the chances of atrial fibrillation that is causing symptoms being detected. It would also mean that preventative treatment is not delayed. Alternatively, if symptoms are present but no arrhythmia can be seen on an ECG this can help to rule out atrial fibrillation as a cause. The clinical experts also commented that many GP practices cannot do a 12-lead ECG immediately because they do not have the equipment on site or because staff are not available to do, or interpret, the test. Ambulatory

ECG monitoring may need to be done, which needs multiple visits to a hospital. The committee concluded that the availability of lead-I ECGs could improve access to testing for people with symptoms of atrial fibrillation.

Clinical effectiveness

5.3 The committee considered the studies included in the diagnostic accuracy review. It noted that the external assessment group (EAG) had concerns over the applicability of several of the studies because lead-I ECG traces were interpreted by the device's algorithms alone, rather than by a trained healthcare professional. It noted that the companies stated that the algorithms alone should not be used to diagnose atrial fibrillation. Clinical experts highlighted the importance of having trained healthcare professionals review ECG traces generated by the lead-I ECG devices. This is to confirm or exclude atrial fibrillation and to check any algorithm outputs, and therefore inform treatment decisions. The committee noted that the trained healthcare professionals interpreting the ECGs in the identified studies were generally cardiologists or electrophysiologists, who may be more experienced in interpreting ECG traces than GPs. In 1 study (Williams et al. 2015), in which the interpreter was a GP with a special interest in cardiology, specificity estimates were lower than those obtained when a cardiologist interpreted the trace. Also, accuracy estimates of the devices varied between the 2 electrophysiologists in Desteghe et al. (2017), suggesting that interpretation of the lead-I ECG traces is likely to be subject to inter-observer variability. The committee concluded that it was important that decisions about treatment based on lead-I ECG traces are made only after review by a trained healthcare professional, because this may have a substantial effect on false results.

5.4 The committee noted that the populations varied in the studies included in the EAG's diagnostic accuracy review. Most of the studies were done in people who did not report symptoms of atrial fibrillation, but who were attending cardiology services because of an underlying cardiac problem. It recalled that the EAG had highlighted this as a generalisability issue. The clinical experts explained that because the populations in the included studies tended to be older, the burden of atrial fibrillation would

be expected to be greater than in a truly asymptomatic population. The committee considered that the absence of studies that were directly applicable to the population in this assessment was not ideal. But it concluded that the available studies provided a reasonable estimate of the ability of the devices to correctly identify atrial fibrillation.

5.5 The committee considered the diagnostic accuracy data that were available for each of the devices. It noted that 5 studies were available for Kardia Mobile, 3 for MyDiagnostick and 1 for Zenicor-ECG. The committee also noted that there was uncertainty about whether current versions of the algorithms had been used in the diagnostic accuracy studies for the lead-I ECG devices. Most of the studies compared each of the devices with a 12-lead ECG and did not include formal comparisons of the devices. There was 1 study (Desteghe et al. 2017) that assessed concordance between MyDiagnostick and Kardia Mobile and reported no statistically significant difference. The committee concluded that the available accuracy data were limited and were not sufficient to assess differences in accuracy between the lead-I ECG devices.

5.6 The committee considered the reference standard used in the identified diagnostic accuracy studies: a 12-lead ECG done within about 6 hours of the lead-I ECGs. It noted that the comparator for this assessment was a 12-lead ECG done several days after the initial GP appointment where the irregular pulse was detected. The EAG identified no studies showing that lead-I ECGs increased detection of atrial fibrillation when compared with 12-lead ECGs done later after an irregular pulse was detected. It noted that studies identified by the EAG that reported diagnostic yield of atrial fibrillation were not done in a population who had symptoms, which is the focus of this assessment. The committee recalled that the potential value of the devices in this context was increased detection of atrial fibrillation, particularly paroxysmal, compared with a 12-lead ECG done later (see section 5.2). It concluded that the identified data did not allow the committee to assess the likely clinical effect of the lead-I ECG devices in increasing detection of atrial fibrillation compared with current practice (that is, a 12-lead ECG done later).

Cost effectiveness

5.7 The committee considered the cost per use of the lead-I ECG devices assumed in the model. It heard that the lifespan of MyDiagnostick was incorrect in the original report, but noted that the EAG had corrected this. The committee questioned the expected average number of people seen by a full-time GP per year that the EAG had used to estimate the cost per use of the devices, noting evidence from NHS Digital that the average number of people per GP is potentially higher. The EAG commented that its estimate was conservative and that if the average number of people per GP was higher this would reduce the cost per use of the devices and improve the cost-effectiveness estimates. The committee also questioned whether the model included the costs of training to use the device. The EAG explained that this was not explicitly included, but it had looked at the effect of increasing the costs of using the lead-I ECG devices and the cost-effectiveness estimates were robust to increases in the costs per use. The committee concluded that, although there were uncertainties in the costs per use assumed in the model, they were not a key driver of the results.

5.8 The committee discussed the costs associated with interpreting the lead-I ECG traces in practice and considered whether these had been adequately captured in the model. It noted its conclusion that the ECG traces from the devices need to be interpreted by a trained healthcare professional to diagnose atrial fibrillation and make decisions about treatment (see section 5.3). The clinical experts explained that there is likely to be wide variation in the ability of GPs to interpret ECGs, and that some practices may use centralised services for this. The committee concluded that there was uncertainty about how lead-I ECGs generated in primary care would be interpreted in practice, and therefore the effect on staff time and costs associated with introducing lead-I ECGs into primary care. Further research was recommended to assess this (see section 6.2).

5.9 The committee considered the risk of bleeding associated with anticoagulant treatment, and noted that the model assumed that all patients have direct oral anticoagulants. It noted that people incorrectly identified as having atrial fibrillation by the lead-I ECG devices in the

model (false positive results) were assumed to have anticoagulants, and so were at risk of bleeding. The clinical experts explained that false positive results were likely to be caused by atrial ectopy, a benign condition that is not associated with an increased risk of stroke. They also commented that this group of people was likely to continue anticoagulants over the longer term, unless they chose to stop treatment. The committee questioned whether the risk of bleeding had been adequately captured in the analyses. The EAG explained that the model did allow for people to have bleeding events, and that a scenario analysis in the addendum including a quality-adjusted life year (QALY) decrement for minor bleeds had very similar results to the base-case analysis. The committee noted that the EAG's model did not account for any excess mortality in people who had a haemorrhagic stroke because of anticoagulants. The EAG commented that the increase in the number of bleeds in the model caused by adopting lead-I ECGs was very small. The clinical experts commented that lead-I ECG traces are reviewed by trained healthcare professionals, which helps to minimise the risk of false positive diagnoses. The committee concluded that there was some uncertainty about whether the model had captured all the adverse effects caused by anticoagulants.

5.10 The committee noted that the model was sensitive to an assumption about the proportion of cases of atrial fibrillation that are paroxysmal. The EAG explained that because of a lack of evidence this had been assumed to be 50% in the base case. The clinical experts commented that about 25% of atrial fibrillation is likely to be paroxysmal, and that the proportion in the modelled population is unlikely to be less than this. If the proportion of paroxysmal atrial fibrillation was set to 25% in the model, the incremental cost-effectiveness ratio (ICER) for Kardia Mobile compared with the standard pathway was about £7,500 per QALY gained, an increase from £1,060 per QALY gained in base case 1, in which it dominated the other lead-I ECG devices. As the proportion of paroxysmal atrial fibrillation was decreased the ICER increased, to around £250,000 per QALY gained when the prevalence was set to 0. The committee concluded that because there were no data on the proportion of people with symptomatic atrial fibrillation that is paroxysmal the cost-effectiveness estimates were highly uncertain.

5.11 The EAG commented that most of the patient benefits in the model (from the use of the lead-I ECG devices compared with the standard pathway) came from an estimated increase in detection of people with paroxysmal atrial fibrillation. However, the committee recalled that no clinical evidence had been identified that showed that lead-I ECG devices increased the detection of people with atrial fibrillation compared with a later 12-lead ECG in practice (see section 5.6). The EAG had made assumptions in the model to estimate the effect of the likely increase in detection of paroxysmal atrial fibrillation associated with the lead-I ECG devices. However, because of a lack of data, it was unclear whether this increase would occur in clinical practice. The committee concluded that although there is plausible potential for the lead-I ECG devices to be cost effective when used for single time point testing in primary care (for people with signs and symptoms of atrial fibrillation with an irregular pulse), there was insufficient evidence at present to determine if the predicted benefits of using the devices would be realised in practice. The committee considered that further research would help to address this (see section 6.1).

5.12 The committee considered the usability of the devices and noted that the EAG identified several studies reporting that the devices were easy to use and were liked by patients and healthcare professionals. However, it noted that 1 study (Desteghe et al.) reported that up to 7% of people were not able to use the devices because they were unable to hold them as recommended by the companies. A patient expert submitted comments that some people may need help in holding the devices while a recording is taken, for example people who have had a stroke or people with arthritis. The committee concluded that healthcare professionals should bear this in mind when using the devices and encouraged the companies to improve the usability of their devices for these groups of people.

5.13 The committee considered the results of the fully incremental economic analyses (see sections 4.43 and 4.46). It noted that all lead-I ECG devices were dominated by Kardia Mobile (that is, using the Kardia Mobile cost less but produced more QALYs). However, the committee recalled its earlier conclusion that the available accuracy data for the lead-I ECG devices were limited and were not sufficient to assess

differences in accuracy between the lead-I ECG devices (see section 5.5). It also noted that the Kardia Mobile did not dominate in all simulations in the probabilistic sensitivity analysis. The committee concluded that there was considerable uncertainty about the relative cost effectiveness of the different lead-I ECG devices, and that a conclusion about which device was most cost effective could not be made from the available data.

Research considerations

5.14 The clinical experts explained that lead-I ECG devices were increasingly being used in primary care settings. The committee noted that Academic Health Science Networks (AHSNs) are assessing the effect of introducing lead-I ECG devices into primary and community care, although their project is broader than the scope of this assessment. The committee considered consultation responses on the AHSN project. It noted that data collected as part of the project may be relevant to the population covered by this guidance and could help answer some of the uncertainties identified on the system impact of adopting the devices (see section 6.2). Clinical experts explained their processes to ensure appropriate governance of patient information when using these devices to detect atrial fibrillation. The committee noted the importance of this and concluded that centres should ensure appropriate information governance is in place for these devices.

5.15 The committee heard that the focus of the AHSN project is to evaluate the extent of spread and adoption of the mobile ECG technology and to describe the optimum environment for implementing a national procured innovation. It is not an evaluation of the technology itself. The committee concluded that data collected as part of the AHSN project were unlikely to resolve uncertainty about the extent of any increased detection of atrial fibrillation by the devices compared with current practice (see section 6.1) and that further research would be needed to address this.

6 Recommendations for further research

6.1 The committee recommended further research to determine if using the lead-I electrocardiogram (ECG) devices in primary care for people with signs or symptoms of atrial fibrillation, and an irregular pulse, increases the number of people with atrial fibrillation (including paroxysmal) detected, compared with current practice (that is, a 12-lead ECG done later). The committee considered the feasibility of collecting data to see if using the lead-I ECG devices increased the detection of atrial fibrillation that would be missed if only 12-lead ECGs done later were available. It noted that even if a lead-I ECG is used and atrial fibrillation is detected, a subsequent 12-lead ECG would still be done to check for structural cardiac abnormalities and inform further management decisions. The committee concluded that practices using lead-I ECG devices could determine the number of additional cases of atrial fibrillation detected by the devices. This can be done by identifying people with a confirmed positive lead-I ECG for atrial fibrillation who subsequently had a 12-lead ECG that was negative because the atrial fibrillation had stopped. The committee also considered that data collected on the time between the initial lead-I ECG and the subsequent 12-lead ECG would be useful.

6.2 The committee recommended that data should be collected to evaluate the system impact of adopting the lead-I ECGs on both primary and secondary care. In particular, data should be collected on how ECGs generated by the devices would be interpreted in practice, including staff time needed to interpret the ECG traces and associated costs.

7 Implementation

NICE will support this guidance through a range of activities to promote the recommendations for further research. The research proposed will be considered by the NICE Medical Technologies Evaluation Programme research facilitation team for the development of specific research study protocols as appropriate. NICE will also incorporate the research recommendations in section 6 into its guidance research recommendations database and highlight these recommendations to public research bodies.

8 Diagnostics advisory committee members and NICE project team

Committee members

This topic was considered by the diagnostics advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the test to be assessed. If it is considered there is a conflict of interest, the member is excluded from participating further in that assessment.

The minutes of each committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Additional specialist committee members took part in the discussions for this topic:

Specialist committee members

Dr Stuart Bennett
GP with special interest in cardiology, Ainsdale Medical Centre

Dr Richard Blakey
GP with special interest in cardiology, The Community Cardiology Service

Dr Matthew Fay
GP, clinical director, Affinity Care

Dr David Fox
Consultant cardiologist/cardiac electrophysiologist, North West Regional Cardiac Centre, Wythenshawe Hospital, Manchester University NHS Foundation Trust

Miss Rebecca Gardner
Lay specialist committee member

Mrs Catherine Ross
Head of clinical leadership, NHS England

Dr Mark Tanner
Consultant cardiologist, honorary clinical senior lecturer, Western Sussex Hospitals and National Heart and Lung Institute, Imperial College London

NICE project team

Each diagnostics assessment is assigned to a team consisting of a technical analyst (who acts as the topic lead), a technical adviser and a project manager.

Thomas Walker
Topic lead

Rebecca Albrow
Technical adviser

Donna Barnes
Project manager

ISBN: 978-1-4731-3400-3

Accreditation